PIGMENTARY DISORDERS

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Melanin and Pigmentary Disorders

Abnormalities in pigmentation are common and frequently produce considerable stress in the patient since they affect appearance. Some of these concerns are purely cosmetic and other pigmentary changes, as with lupus, can signal serious underlying disease. Pigmentary disorders all relate to the amount of the skin pigment melanin. Disorders having excess melanin are known as hyperpigmentary or hypermelanotic diseases. Those with too little melanin or loss of melanin are termed hypopigmentary or hypomelanotic. Hair contains melanocytes and pigment loss here can cause loss of hair pigment with white hair. Melanin is contained within cellular organelles called melanocytes. These are pigment-producing cells found in the basal layer of epidermis. The melanin is then transferred out of the melanocyte packaged in melanosomes to the keratinocyte in the outer layer of epidermis. In caucasians, melanocytes are bound to the cell membrane of the keratinocyte and are of smaller size. In people of color, the melanosomes are dispersed throughout the cell body (cytoplasm) of the keratinocyte and are larger than in whites. Asians and red-haired persons have a slightly different chemical type of melanin.

Melasma

Melasma is a very common hyperpigmentary disorder that affects sun-exposed areas in women. Sun exposure and tanning make it worse. The hyperpigmented areas occur on the cheeks, central face, forehead, upper lip and chin. It can occur in men but males compose only 10% of cases. It is usually related to hormone excess, as in pregnancy, oral contraceptive pill use, and endocrine disorders. It may be associated with some cosmetics, some medications (dilantin, oral contraceptives) and severe liver disease. In women taking oral contraceptives, about 30% develop melasma. Postmenopausal women on estrogens do not usually develop melasma. It is treated with skin lightening agents, camouflage makeup, strict avoidance of tanning, and stopping any potential causative medicines.

Vitiligo

This disease causes loss of pigment by destroying melanocytes. The cause is actually unknown, although genetics is frequently postulated as a cause since 30% of people with vitiligo have an affected family member somewhere in their family tree. Affected families have an increased incidence of graying of the hair. All races are affected but it is more noticeable in darker complexions.

Men and women are equally affected. One to two million Americans have vitiligo and it is found in 1-2% of the world's population. The most common age of onset is the first two decades of life. Sometimes spontaneous remission occurs and repigmentation is seen. The most common areas affected are the face, back of the hand, wrists, armpits, central abdomen and genitalia. Childhood vitiligo is seen in children under 12 years and is different from the other type in that depigmentation frequently occurs in long segments.

Treatment is very difficult. Some treatments include PUVA (psoralens plus ultraviolet A light exposure), topical steroids, surgical treatments of various grafting or micrografting types. Stem cell therapy may have potential for the future.

Tinea Versicolor

Tinea versicolor is also called Pityriasis versicolor and is a superficial infection of the stratum corneum caused by the yeast, Malassezia furfur. It is found throughout the world and in all races, although it favors tropical climates. It also tends to be more severe in the tropics. The small circular hypopigmented lesions are most commonly found on the torso and may be very numerous. Affected areas do not tan well and become more noticeable in the summer or with tanning. Eradication of the infection is difficult and recurrence rates within two years are 60-80%. Topical antifungal medicine is used to treat the infection.

Injury or Inflammation

Any injury to the skin may result in pigmentary changes. These can cause increased or decreased areas of pigment production. Inflammation may be conceptualized as a type of injury so this also may lead to pigmentary abnormalities. This is an uncommon but well-recognized complication of laser therapy in plastic surgery.

Pigmentary abnormalities due to injury seem to be more common in individuals with more natural pigment than in fair-skinned individuals.

Acanthosis Nigricans

This is a disorder of increased pigment. A velvety hyperpigmentation occurs in large patches. The patches are found, in descending order of frequency, in the axillae (armpits), neck, groin, breast folds, inner elbows, back of the knees, and around the mouth. Interestingly, the patient usually refers to the appearance of the initial lesion as a “dirty area”, although it is certainly not dirty. Skin thickening occurs as the disease advances. There is an association with obesity and the disease worsens as the patient gains weight. Acanthosis nigricans occurs in 13% of African Americans, 6% of Latin Americans, and about 1% of Caucasians.

There is a variant of Acanthosis Nigricans disorder with onset in adulthood that is associated with internal malignancies. The rapid onset of this disorder or large, generalized lesions should prompt the physician to search for the underlying malignancy.

Medicines such as insulin, nicotinic acid, diethylstilbestrol, glucocorticoids, oral contraceptive pills, and methyltestosterone can be associated with the development of acanthosis nigricans.

Treatment is weight loss if the cause is obesity. In all other types, treatment is extremely difficult although various topical therapies (topical retinoids, topical corticosteroids) have been tried.

Café-au-Lait Macules

These larger areas are brownish in color (café-au-lait or coffee-with-cream color). They have irregular margins and may be from 0.2 to 20 cm in diameter. They have an association with a potentially serious genetic disease, neurofibromatosis.

Product Recommendations

iS CLINICAL® products that help treat pigmentary disorders include: SUPER SERUM™ ADVANCE+ and ACTIVE SERUM™.

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HYDROQUINONE

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Topical hydroquinone is used frequently throughout the world as a skin bleaching agent. Hydroquinone for cosmetic use is chemically synthesized. It may be found in concentrations up to 15% or more but a doctor's prescription is required by the FDA (United States) for preparations containing concentrations above 2%. The CIR Expert Panel states hydroquinone should not be used in "leave-on" cosmetic formulations. In spite of this, internet sites can easily be found that offer topical hydroquinone in concentrations over 2% and very commonly as high as 4% or more.

The World Health Organization of the United Nations states: "It is recommended that over-the-counter sales of creams containing hydroquinone be restricted. Health education programs should be developed to discourage the use of hydroquinone-containing creams…"

Hydroquinone was originally introduced many years ago as a less toxic alternative to mercury-based bleaching agents, which were extremely toxic. Attention is now being focused on the potential toxicities and adverse effects of hydroquinone itself.

MECHANISM OF ACTION

Hydroquinone is easily absorbed into the skin and its absorption increases dramatically when alcohols are present in a topical preparation. Hydroquinone reacts with the functional parts of individual cells and effects cellular metabolism. Hydroquinone has cytotoxic (cell-killing or cell-damaging) activity on the pigment-producing cell of the skin, the melanocyte, as well as on many other cell types. The cell-toxic activity of hydroquinone is caused by a free-radical oxidation mechanism. Free radical development has the potential to damage the melanocyte on its own and may also damage neighboring cells or their physical structures. Because this free-radical effect also harms the genetic material within the pigment-producing cell, it can result in the development of a cancerous (malignant) cell.

COMPARISON WITH OTHER AGENTS

Arbutin, which is of plant origin, decreases the production of the skin pigment melanin. Arbutin inhibits an enzyme called tyrosinase which is required for one of the chemical steps in melanin formation. This inhibition of pigment formation occurs without cytotoxic (cell-damaging) activity.

Kojic acid, of plant origin and an alpha-hydroxy acid, is another enzyme inhibitor of tyrosinase. It decreases pigment production in a manner similar to arbutin. Adding both kojic acid and arbutin to a product causes a potentiation of the lightening effects from both, particularly when the product is used during daytime hours.

Laser treatments have been used for pigmentation irregularities but require a surgical procedure and have their own list of potential complications. Laser treatments should be administered under the direction of a physician regarding risks and benefits.

The skin's pigmentation process may be modified by affecting any step in the pigmentation process. Several of these steps involve the melanocyte but there are several other required steps independent of the melanocyte. The single intended site of action of hydroquinone is its cytotoxic effect on the melanocyte. In addition to damaging or killing the melanocyte, hydroquinone also induces considerable secondary inflammation on surrounding skin structures.

POTENTIAL ADVERSE EFFECTS

It was once thought that concentrations of hydroquinone of 2% or less had negligible potential for adverse effects. We now know this is not true, as the medical literature reports problems occurring with lesser

concentrations. The topical side effects after hydroquinone application are thought to be related to its mechanism of cytotoxicity. Another earlier myth was that only heavily pigmented skin suffered from adverse effects related to hydroquinone use. This also is untrue, as side effects in Asians, Hispanics, Caucasians and Blacks with less pigmentation have been reported in the medical literature. Applying hydroquinone to skin and then exposing the skin to sunlight markedly increases potential toxicity. Additionally, hydroquinone is systemically absorbed through the skin with measurable amounts appearing in urine after topical application. Orally ingested hydroquinone is very rapidly absorbed by the GI tract and is known to incite kidney and liver damage. In the presence of moisture and at room temperature, hydroquinone metabolizes to quinone which can cause serious issues such as eye irritation, leading to conjunctivitis (red eye) and erosions of the cornea (open sores over the central eye). The potential adverse effects involving inflammation (redness) and cell damage (related to free radical damage) potentially result in severe reactionary hyperpigmentation. The potential development of malignant cells is also of great concern.

Inflammation

Redness (also called erythema), an indicator of inflammation, reliably occurs with exposure to hydroquinone in concentrations of 2% up to 5% in a tested population when applied 5 days per week for 13 weeks. This redness dissipates after the treatment is stopped but the skin has suffered the effects of inflammation during the exposure period. Visible inflammation is found in the majority of users with any concentration of hydroquinone. Since the substance is toxic to cells, even if redness cannot be seen with the naked eye, there is ongoing inflammation accompanying the cell damage associated with the substance. This is a type of irritant dermatitis, or skin inflammation caused by an irritating substance.

Irritant or Allergic Dermatitis

This is an allergic response to a substance to which the skin has become sensitized. It may begin with an inflammatory response but the subject can become so sensitive to the product that they develop skin inflammation when only a tiny amount of substance is applied to the skin or even if previously compatible substances are applied.

Systemic Absorption

Hydroquinone is readily absorbed through the skin and can be detected in urine as the intact parent substance (rather than a metabolite) after the 2% cream is applied. The evidence relating to kidney damage of orally ingested material raises concerns here, considering that hydroquinone applied to the skin must get through the blood stream and the rest of the body in order to be found in urine. This raises other questions about the cancer-causing (malignant) potential and other cell-damaging (cytotoxic) properties of hydroquinone that could occur with systemic absorption (passage through the skin to the remainder of the body). Blood cell toxicity and leukemia have been associated with hydroquinone absorbed throughout the body.

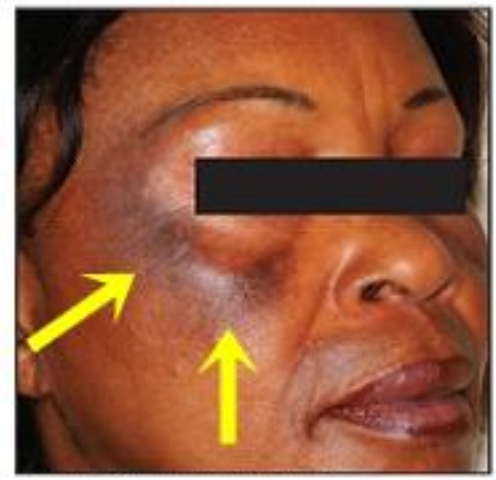
Dyschromia

A literal translation of this term would be "abnormal discoloration". Even though hydroquinone is applied for skin bleaching, its end result can be the formation of large patches of uneven skin color. Dyschromia is very unsightly and difficult to treat. Since hydroquinone has itself been the cause of the dyschromia it is not an effective treatment. Laser treatment is sometimes prescribed but is not always effective, requires a surgical procedure, and has its own potential complications.

Exogenous Ochronosis

This is a type of dyschromia that is particularly serious. Furthermore, it is usually impossible to control once it has developed. Another variant of this skin pigment disorder is inherited and can be associated with malignancies, but this exogenous (meaning 'caused outside the body') type is associated with topical hydroquinone use. It involves increased pigmentation of any skin exposed to hydroquinone. The majority of patients suffering from ochronosis have heavier genetic melanin production. Ochronosis is especially frequent in South African Blacks, who sometimes use as high as

27% concentration of hydroquinone in skin bleaching products. This disorder can also occur in Asians, Hispanics and Caucasians with hydroquinone use. Treatment is extremely frustrating because improvement occurs so slowly or not at all with this debilitating condition. The photo below illustrates the debilitating and permanent effects of ochronosis.



Macular hyperchromia, a type of ochronosis shown in the photo above, is an increased pigmentation of the area surrounding the eyes. It occurs in up to one-third of African Blacks using hydroquinone skin-bleaching products. Improvement in this condition is extremely slow.

Striae

Striae are the "stretch marks" that often occur with pregnancy and rapid weight gain. Their appearance has also been associated with the use of hydroquinone. They are permanent and result from skin inflammation and resultant scarring related to hydroquinone use.

Very Rapid Re-Pigmentation

This condition described in the medical literature relates to the disease vitiligo that very rapidly re-pigments after the use of hydroquinone is discontinued. Vitiligo is a skin disorder manifested by areas devoid of pigment that appear as very pale skin pigmentation mixed with normally pigmented areas. A common treatment is to apply skin bleaching agents to the normally pigmented skin encouraging loss of melanin and a blending with the depigmented skin. Improvement may occur but is very rapidly lost within a few weeks as the skin rapidly re-pigments.

Fingernail Discoloration

Fingernails may develop a brownish discoloration with 4% hydroquinone-containing skin bleach that also contains tretinoin. When use of the cream is stopped, the nail discoloration may gradually go away.

Hydroquinone Neuropathy

A single case report in the medical literature involves the gradual development of increasing weakness in the legs associated with topical hydroquinone use. This patient used 2 hydroquinone bleaching preparations for about 4 years. She stopped using the creams and 4 months later, her leg weakness resolved.

CURRENT USE

Topical hydroquinone in concentrations in excess of 4% can still be found on black markets particularly in the developing world. Hydroquinone is prescribed by physicians in the United States and other countries, especially in combination with topical steroids which are hoped to lessen the side effect profile. Most physicians prescribe hydroquinone for brief use and expect it will be used by the patient on a temporary basis. However, it can be difficult for the patient to transition off of hydroquinone without return of pigmentation or development of reactionary hyperpigmentation. This is especially problematic for the hydroquinone user when the regimen is not physician-guided. Because of this and the other factors previously discussed herein, both consumers and professionals are much more interested in non-hydroquinone lightening products.

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iS CLINICAL® WHITE LIGHTENING™ WHITE PAPER

FACTORS AFFECTING PIGMENTATION & MELANIN SYNTHESIS

There are different types of melanin. Pheomelanin is yellow-orange and is found in those with blond and red hair. Eumelanin is dark brown to black and is found in those with dark hair.

The complex process of melanin production within melanocyte cells of the skin is only part of the pigmentation process. Melanosomes are organelles within melanocytes that synthesize melanin and also serve as a transport vehicle for melanin. The chemical synthesis of melanin within the melanosome includes several steps. The most important step is the "rate limiting" step, which is dependent on the enzyme tyrosinase. The rate-limiting step is the slowest of the chemical reactions in the series of melanin production. It therefore determines the overall rate at which melanin can be synthesized.

After melanin production, melanosomes are then transferred from melanocytes in the basal layer of the epidermis to the upper layer of keratinocytes. Once melanosomes arrive in keratinocytes they are subject to degradation (hydrolysis) and loss of pigment. Keratinocytes move upward into the stratum corneum as they lose pigment, arriving in the outermost layer of the skin when they contain no more melanosomes and are devoid of pigment. The degradation of melanosomes in keratinocytes begins almost immediately in Caucasians, is much slower in Asians and slowest in those of darker complexions.

Any injury to the skin may result in pigmentary changes. These can cause increased or decreased areas of pigment production. Inflammation is a consequence of injury and excess inflammation commonly leads to pigmentary abnormalities. This is an uncommon but well-recognized complication of laser therapy in plastic surgery. Pigmentary abnormalities due to injury seem to be more common in individuals with more natural pigment than in fair-skinned individuals. Asian skin seems to be more sensitive to injury from exogenous chemical exposure or mechanical stress. This is due to a thinner stratum corneum and denser sweat glands. Injury and inflammation involve pathways strongly affected by oxidative stress or free radical reactions.

Induction of the skin's response of hyperpigmentation is via signaling by protease-activated receptor-2. This receptor and its accompanying protease are both increased in Asians and other persons of color. This natural genetic upregulation explains why Asians pigment more readily to any stimulus. The higher amounts of melanin found in the skin of Asians and other persons of color is at least somewhat photoprotective, thus explaining why Caucasians exhibit earlier wrinkling and skin sagging in genetic comparisons.

Sunburn is a type of injury that commonly leads to excess and uneven pigmentation in individuals of all races and ages. Solar exposure of any sort (even mild) strongly induces melanin formation. With exposure to the sun's rays, the movement of melanin upward in the skin from melanocyte to keratinocyte is more dramatic in Asians and all persons of color.

It must be strongly emphasized that, in addition to using a lightening product, use of a very effective sunscreen and avoiding unnecessary sun exposure will maximize desired results.

Understanding the above processes gives potential avenues through which pigmentation may be modified. The five known potential routes of control include the reduction of melanin with tyrosinase inhibitors, the interruption of the transfer of melanin between melanocyte and keratinocyte, reduction of inflammation, the use of antioxidants and exfoliation. The lightening effects of an end-product are improved as the number of physiologic processes affected by the product is increased.

CLINICAL IMPROVEMENT IN PIGMENTATION WITH WHITE LIGHTENING™ SERUM

STUDY OBJECTIVE

The effect of WHITE LIGHTENING™ SERUM on a group of subjects with areas of hyperpigmentation was evaluated. The subjects were evaluated by a clinical investigator and were asked a series of questions regarding their opinion of the product's actions, including any general lightening effects provided by the product.

STUDY DESIGN

WHITE LIGHTENING™ SERUM was applied twice daily in test subjects over a 12-week period. A total of 31 subjects were evaluated, seven of which were Asian. The age range was 40-80 years. Subjects were limited to Fitzpatrick Types I, II and III that had been diagnosed with pigmentary irregularities such as hyperpigmented areas, "age spots," and/or melasma involving the face, hands and/or forearms. Subjects were evaluated on a regular basis and data was recorded for evaluation at the beginning of the study period and after completion at 12 weeks of use. Exams by an experienced clinical investigator of 3 separate representative areas per subject were performed. The intensity of pigmentation was graded and the size of hyperpigmented areas was recorded. Patients also answered a number of evaluative questions regarding the actions of the product. Digital photos were taken with a special device for photo documentation of the skin. Software for picture analysis of this data was used and the total area and degree of pigmentation for each area calculated. The data was statistically evaluated using the Wilcoxon test and the Kolmogorov-Smirnov tests for statistical analysis.

SIGNIFICANCE OF THE STUDY

Melanin production in melanocytes may be induced or stimulated in photodamage with sun exposure and in aging, as indicated by the development of pigmentary irregularities and "age spots." Persons with darker skin have melanocytes that are more quickly and easily "tuned up" by any stimulus. For example, Asian skin is more susceptible to pigmentary irregularities early-on in life because it is more sensitive to damage and responds more promptly to it. Because of these differences in sensitivity to damage, it was important to include a variety of skin types in this study. Fitzpatrick Types I, II and III were included.

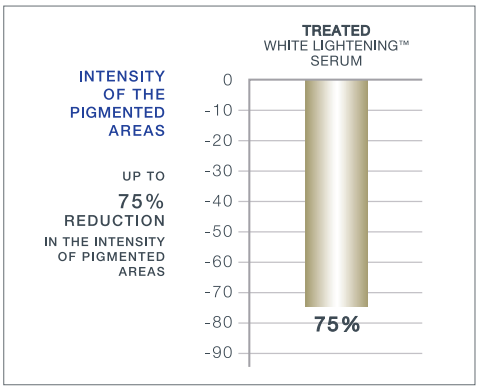
In addition to a lightening formula, sun protection is an essential first step for any lightening regime. A good sunscreen must always be used when going outside or when near windows. Avoidance of sun exposure as much as possible is very important. After these important steps are taken to modify sun exposure, if the individual still finds it desirable to control pigmentation, it is important to offer options that are both safe, i.e. lacking toxicity, and effective. Since solar exposure in any amount is a strong stimulator of melanin synthesis, use of sunscreen should continue in concert with these other options.

Although many people experience a need for pigment-controlling products, adequate pigment modulation is, in fact, difficult to achieve. In the past, such products were often associated with unacceptable side effects. These side effects ultimately resulted in a more unsightly appearance with very uneven and darker areas of pigmentation. WHITE LIGHTENING™ SERUM offers break-through technology that is quite unique in its ability to effectively lighten hyperpigmented areas and avoid unwanted side effects.

RESULTS AND CONCLUSIONS

There was a clear and very high statistical improvement when using WHITE LIGHTENING™ SERUM on the face, forearm and hands. Subjects themselves reported that the product was quite effective and that they would choose to continue using it. There were no adverse reactions, sensitivities, redness or irritation to the product in any of the subjects.

SIZE AND INTENSITY OF PIGMENTED AREAS

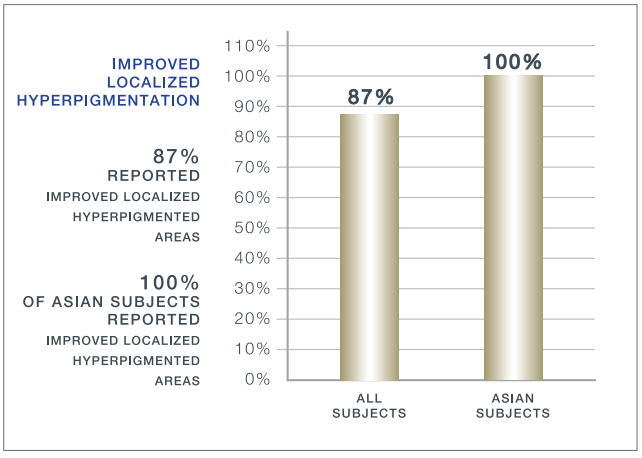


The intensity of pigmentation when measured by instrumentation decreased by up to 75% in the subjects. Size of the pigmented areas decreased by up to 21% when measured precisely. The subjects themselves reported a very pronounced reduction in severity of pigmented areas. This is thought to be related to the greater concomitant decrease in darkness of pigmentation, making the size of the areas seem much smaller to the subjects themselves because the entire area of testing was fainter.

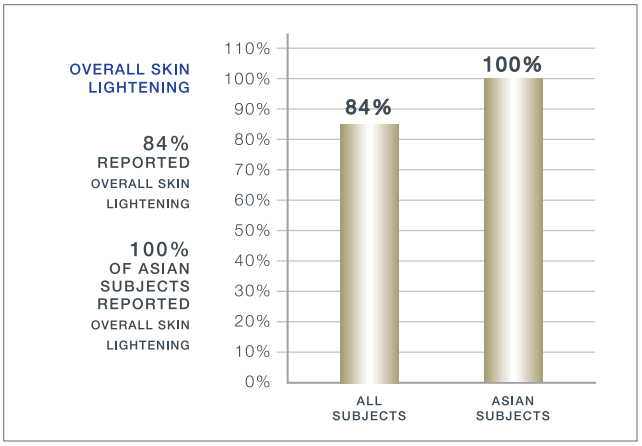
One hundred percent of the melasma subjects thought their overall skin was lighter and their pigmented areas improved.

SUBJECT ASSESSMENT OF THE PRODUCT

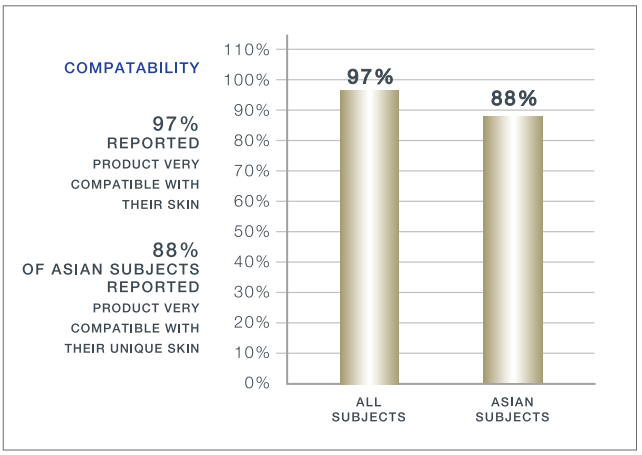
This section gives the opinion of the subjects themselves on the effectiveness of WHITE LIGHTENING™ SERUM.



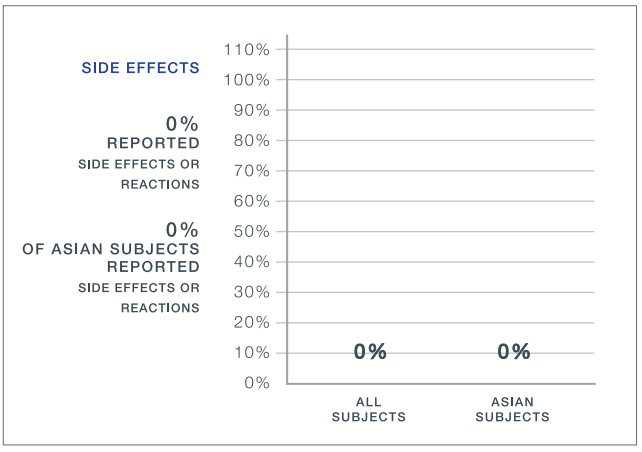
Of all subjects, 87% reported the product improved localized hyperpigmented areas. Of Asian subjects, 100% reported the product improved localized hyperpigmented areas.



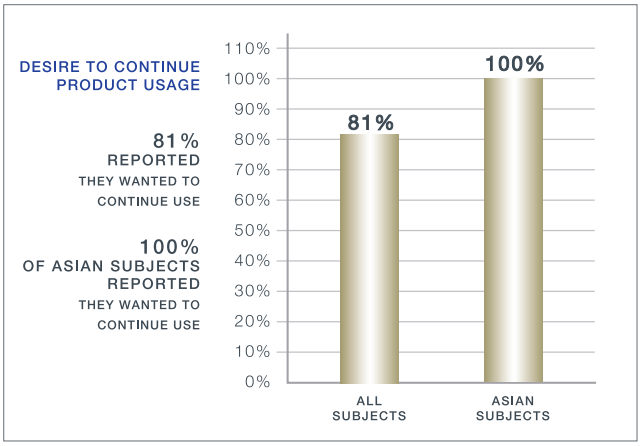
In the entire group, 84% of all subjects reported overall skin lightening and 100% of Asian subjects reported overall lightening of their skin. No "haloing" outlining the area of use or uneven pigmentation was reported by any subject.



Of all subjects, 97% thought the product was very compatible with their individual skin. Of Asian subjects, 88% thought the product was very compatible with their unique skin.



There were no side effects or reactions whatever to the product. No subjects reported redness, irritation, rash, dryness, uneven pigmentation or other undesirable effects of the product.



Of all subjects, 81% wanted to continue use of the product. Of the Asian subjects, 100% wanted to continue use of the product in the future.

THE EFFECT OF WHITE LIGHTENING™ COMPLEX ON MELANIN SYNTHESIS

STUDY OBJECTIVE
The cellular effect of WHITE LIGHTENING™ COMPLEX on melanin production by the melanocyte was evaluated.

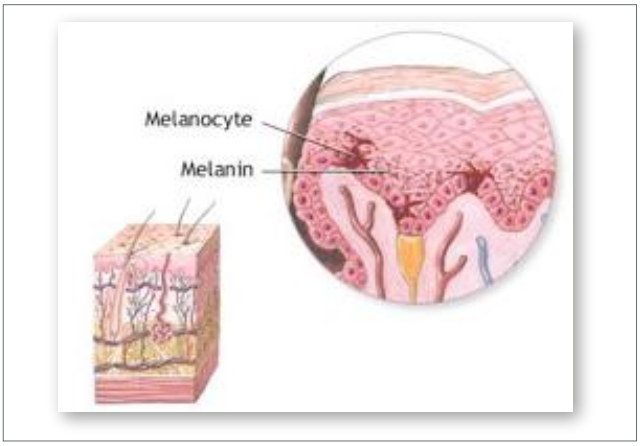
STUDY DESIGN
Melanocytes were exposed to WHITE LIGHTENING™ COMPLEX and melanin synthesis was evaluated. Melanocytes were encouraged to produce pigment by exposing them to theophylline. This widely-accepted method is used by scientists to induce melanin production and test the effectiveness of a substance in suppressing the pigment-producing ability of the melanocyte. To one group of melanocytes, WHITE LIGHTENING™ COMPLEX was applied. To another group of melanocytes, no product was applied. The amount of melanin produced by each group of cells was then exactly determined.

Although the difference in melanin can easily be seen with the naked eye, it is much more accurate to measure the exact amount of melanin produced in the untreated group of melanocytes and compare it with the melanin produced in the group using WHITE LIGHTENING™ COMPLEX. This is performed scientifically using a spectrophotometer. In this case, the instrument very precisely measured the amount of melanin present via the light waves emitted by the melanin.

SIGNIFICANCE OF THE STUDY
Considering the impressive results shown during the clinical study previously described, it would not be surprising to find that WHITE LIGHTENING™ COMPLEX affected melanin synthesis by the melanocyte. This study regarding melanin synthesis provided quantification of any changes in melanin synthesis.

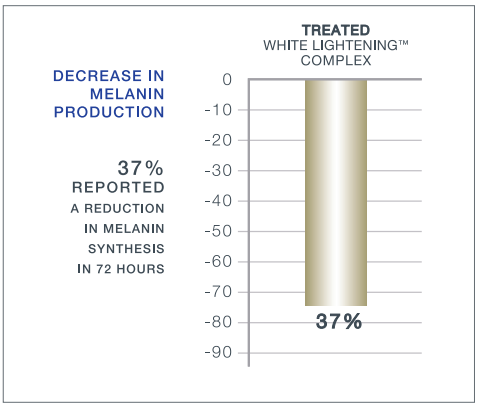
As discussed previously, pigment in the skin is made by melanocytes which produce melanin. Conditions of hyperpigmentation exhibit not only locally increased, but also uneven pigment. In all persons who wish to treat hyperpigmentation of any sort, decreasing pigment production (melanogenesis) by the melanocyte is essential.

A microscopic cross-section of human skin is shown below. Melanocytes in the epidermis are pigment-producing cells that synthesize melanin. Normal melanin production varies according to ethnicity. Melanocytes can be grown in cell culture and the amount of melanin they produce can be determined by precise scientific measurements. In this way, it is possible to evaluate the effectiveness of a lightening product on melanogenesis.



RESULTS AND CONCLUSIONS
Melanocytes grown in "wells" show a clear visual difference in the melanocytes treated with WHITE LIGHTENING™ COMPLEX. In untreated melanocytes, the amount of melanin produced is much greater and the coloration is obviously darker. In treated melanocytes, WHITE LIGHTENING™ COMPLEX decreased melanin production and the coloration seen is much lighter. For the user, this causes skin to be lighter by instructing the melanocyte to produce less pigment.

The graph below shows the decreased melanin production by melanocytes treated with WHITE LIGHTENING™ COMPLEX as compared with untreated melanocytes.



Each control melanocyte (without WHITE LIGHTENING™ COMPLEX) produced 101 picograms of melanin. With WHITE LIGHTENING™ COMPLEX, each melanocyte produced only 64 picograms of melanin. This shows that production of melanin by the cell dramatically decreases when WHITE LIGHTENING™ COMPLEX is applied, even when the melanocyte is stimulated to maximize melanin production (37% reduction in melanin synthesis in 72 hours).

In all persons, melanocytes are stimulated when skin is exposed to the environment. Those with darker complexions have a more intense production of pigment. In conditions indicated by hyperpigmentation, including photodamage, injuries, surgical wounds, aging and melasma, the melanocyte is stimulated to make excess melanin in affected areas of skin. Even the maximally-stimulated melanocyte produces less melanin when WHITE LIGHTENING™ COMPLEX is applied. The user should see a clear clinical improvement in hyperpigmented conditions with WHITE LIGHTENING™ COMPLEX.

SUMMARY OF STUDIES ON WHITE LIGHTENING™ PRODUCTS

The studies performed on WHITE LIGHTENING™ PRODUCTS demonstrate their dramatic effectiveness and safety. A comprehensive lightening regimen must also include use of sunscreen and avoidance of unnecessary sun exposure.

Melanin is produced in skin by melanocytes. The melanocyte may be stimulated by photo damage, aging, other injuries, surgical procedures, scarring or inflammatory processes to increase its production of melanin, resulting in unwanted hyperpigmented areas. Some groups are more sensitive to damage and may exhibit hyperpigmentation at younger ages. Certain cultural preferences may include overall lightening of the skin. There is a demand for lightening products that address these concerns.

An effective lightening product should exhibit clinical improvement in the skin pigment of actual subjects. The subjects evaluated should be quite similar to those expected to use the product. Effects should be demonstrated at the cellular level on melanocytes. There should be absence of toxicity and side-effects in the clinical study. WHITE LIGHTENING™ products conclusively demonstrate these desired clinical and biochemical/cellular effects.

References available upon request.

iS CLINICAL®
COSMECEUTICALS

WHITE LIGHTENING™ COMPLEX

3.3 pH +/- 0.5 30ml £98.00

BRIGHTENING I HYDRATING I REPARATIVE

Featuring an innovative blend of proprietary lightening ingredients and pharmaceutical grade botanicals this unique formula safely and effectively brightens & lightens the skin addressing all 5 mechanisms that are proven to cause hyperpigmentation.

BENEFITS

- Reduces hyperpigmentation
- Lightens, brightens & evens skin tone
- Reduces inflammation
- Moistorises & smooths skin
- Provides Antioxidant protection

KEY INGREDIENTS	INGREDIENT BENEFITS
SALIX ALBA (WILLOW) BARK EXTRACT (source of salicylic acid) 18%	Encourages desquamation by “dissolving” intracellular “cement” with no inflammatory effects. Also deep cleans the pore and removes debris within hair follicles.
GLYCERIN, SQUALINE AND IMPERATA CYLINDRICA ROOT EXTRACT 12%	Proprietary compound that optomizes and reinforces collagen synthesis and moisture absorption in the skin.
HYALURONIC ACID (botanically derived) 11%	Serves as a humectant to attract and bind the skin’s natural moisture increasing cellular hydration.
SACCHARUM OFFICINARUM (SUGAR CANE) EXTRACT (source of glycolic acid) 7%	Desquamation agent: encourages exfoliation of stratum corneum.
VACCINIUM MYRILLUS (BILBERRY) FRUIT/LEAF EXTRACT (source of lactic acid) 5.7%	Desquamation agent with moisturizing properties; enhances exfoliation of the stratum corneum without dehydrating the skin.
ASCOPHYLLUM NODOSUM EXTRACT (norwegian kelp extract) 5%	Interrupts communication between melanocyte and keratinocyte and increases controlled exfoliation, helping to remove pigmented areas.
TETRAHEXYLDECYL ASCORBATE 5%	Antioxidant and free radical scavenger, lightens via inhibition of melanin synthesis, necessary for healthy collagen synthesis, inhibits MMP enzymes.
ALPHA ARBUTIN 2%	Inhibits tyrosinase enzymes that produce melanin, thus controlling hyperpigmentation.
POLYPORUS UMBELLATUS (MUSHROOM) EXTRACT (source of kojic acid) 1.0%	Inhibits tyrosinase enzymes that produce melanin, thus controlling hyperpigmentation. Also exhibits powerful anti-bacterial, anti-microbial and antibiotic properties.
GLYCYRRHIZA GLABRA (LICORICE) ROOT EXTRACT 0.5%	Inhibits tyrosinase enzymes that produce melanin, thus controlling hyperpigmentation. Also exhibits powerful anti-bacterial, anti-microbial and antibiotic properties.

iS CLINICAL®
COSMECEUTICALS

WHITE LIGHTENING™ SERUM

3.4 pH +/- 0.5 15ml, £62 30ml, £105

BRIGHTENING I REPARATIVE I ANTI- ACNEIC

A powerful formula that safely and rapidly lightens hyperpigmented areas while providing significant controlled exfoliation without evident peeling. This lightweight and easily absorbed serum is excellent for overall coverage, or as a targeted boost for problem hyperpigmented areas. It is a concentrated combination of potent botanical ingredients that address hyper-pigmentation on a number of levels, while providing multiple anti-aging benefits.

BENEFITS

- Effectively targets hyperpigmented areas
- Lightens & brightens skin tone
- Faciliates controlled exfoliation of skin

PRODUCT HIGHLIGHTS

As a specialist aesthetic physician, I insist on trying any new product personally before introducing then to patients. My skin has a fair amount of sun damage and freckling. I have only been using White Lightening for 2 weeks and there is a definite improvement in the pigment. Gorden Cohen, MD MBA, CCN, The Face and the Body Institute, South Africa

KEY INGREDIENTS	INGREDIENT BENEFITS
SACCHARUM OFFICINARIUM (SUGAR CANE) EXTRACT (source of glycolic acid) 2.0%	Desquamation agent; encourages the exfoliation of the stratum corneum.
VACCINIUM MYRTILLUS (BILBERRY) FRUIT/LEAF EXTRACT (source of lactic acid) 2.0%	Desquamation agent with moisturizing properties; enhances exfoliation of stratum corneum without dehydrating the skin.
ALPHA-ARBUTIN 1.0%	Inhibits tyrosinase enzymes that produce melanin, thus controlling hyperpigmentation.
SALIX ALBA (WILLOW) BARK EXTRACT (source of salicylic acid) 1.0%	Encourages desquamation by “dissolving” intracellular “cement” with no inflammatory effects. Also deep cleans the pore and removes debris within hair follicles.
POLYPORUS UMBELLATUS (MUSHROOM) EXTRACT (source of kojic acid) 1.0%	Inhibits tyrosinase enzymes that produce melanin, thus controlling hyperpigmentation. Also exhibits powerful anti-bacterial, anti-microbial and antibiotic properties.