elite emergence

A scientific overview of hyperpigmentation treatment and what lies ahead

by Kirsten Sheridan, licensed aesthetician

Hyperpigmentation can affect any skin type or tone. Melasma, post-inflammatory hyperpigmentation (PIH), and solar lentigines are often bundled under the umbrella term of hyperpigmentation. Not all hyperpigmentation presents the same way, so the approach to treatment should not be a one-size-fits-all. To ensure result-driven treatment outcomes, a multistep approach is key.

Before diving into the different causes of pigmentation, how to treat it, and what the future of hyperpigmentation treatment might look like, let's first look at how it develops.

DIVING DEEPER

Pigmentation begins in the specialized cell, the melanocyte, located in the stratum germinativum of the epidermis. Melanocytes are found in a ratio of one melanocyte to 10 keratinocytes spread out along the dermal-epidermal junction. Melanocytes can provide melanin pigment to 36 keratinocytes through dendric legs as far as the stratum spinosum in some instances.

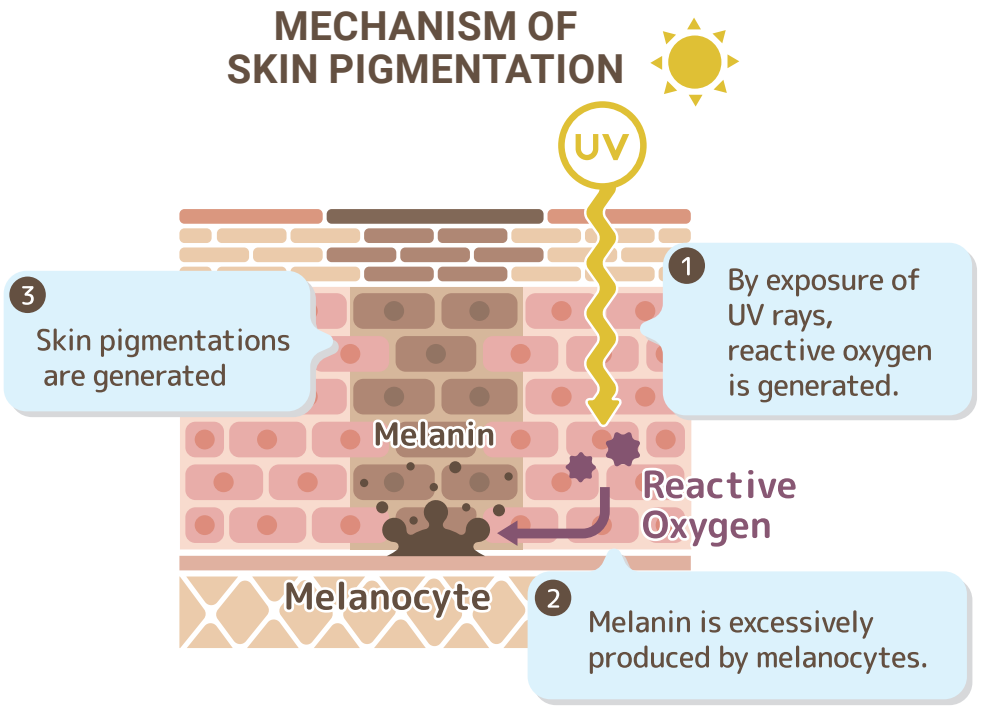
Skin pigmentation is a combination of eumelanin and pheomelanin; more eumelanin is present in deeper skin color and more pheomelanin present in lighter skin color. While the number of melanocytes is the same between dark and light skinned individuals, there are a few differences. Melanosomes that contain eumelanin, referred to as eumelanosomes, have denser pigment; the dendrites of the melanocyte are longer and can reach further up into the layers of the epidermis, as far as the stratum spinosum. Pheomelanosomes containing pheomelanin are much sparser when it comes to pigment. Melanocytes are smaller and their dendrites are shorter.

Ultraviolet exposure may play a primary or secondary role in the formation of hyperpigmentation. While melanin contributes to the color of skin, its main function is to protect the nucleus of mitotic keratinocytes and their DNA. Melanin-filled melanosomes form an umbrella over the nucleus of the keratinocytes. Melanin absorbs the photons of ultraviolet light and disperses as heat, protecting fragile DNA. In response to ultraviolet rays, the melanocytes are triggered by the surrounding keratinocytes to produce more melanin. Eumelanosomes are more effective at protecting DNA and absorbing ultraviolet rays than pheomelanosomes. Ultraviolet exposure is a huge component of hyperpigmentation, whether the cause or a triggering factor. Physical sunscreens with ingredients such as iron and zinc oxide are considered most effective when hyperpigmentation is likely to develop. The need for photoprotection indoors is often overlooked; however, blue light, found naturally in sunlight but also LED and fluorescent lighting, can cause hyperpigmentation. Blue light stimulates reactive oxygen species and causes the breakdown of collagen and elastin over time. Melanocytes sense blue light and regulate pigmentation through opsin 3, a protein, and interact with the melanocortin I receptor (MC1R).

HORMONAL HAPPENINGS

Hormones are another triggering factor for the development of hyperpigmentation. For example, estrogen targets the epidermal melanin unit. It is known that the ratio of melanocytes to keratinocytes is regulated, so if there is an increase in keratinocytes, there should be an increase in melanocytes. This may also vary depending on the sensitivity of the hormone receptors. That is why some individuals are more susceptible to hormonal influences than others.

Melanocyte-stimulating hormone (MSH) are a group of hormones produced in the pituitary gland and in skin. Melanocyte-stimulating hormone directly targets the melanocytes of the epidermis by binding to the melanocortin I receptor (MC1R). In response to ultraviolet



radiation melanocyte stimulation, hormone levels may be increased, resulting in increased melanin production. However, it is not necessarily the level of hormones that causes an issue or results in increased melanin production; it is the sensitivity of the receptors. Individuals may have high blood levels of melanocyte-stimulating hormone but may not struggle with pigmentation disorders. Melanocyte-stimulating hormone levels naturally rise during pregnancy and in those taking birth control pills. Not everyone taking birth control pills or going through pregnancy has a pigmentation issue.

MELASMA & CHOLASMA

Melasma or cholasma is recognizable due to its bilateral hyperpigmented formation across the cheeks, chin, and forehead, often referred to as a "butterfly mask" and occurs predominately in women. Since there is a hormonal sensitivity component to melasma, for example estrogen and progesterone, pregnant women or women on birth control are more likely to experience melasma. Hormone therapies and thyroid disorders may also trigger melasma, and genetics are thought to play a role.

The coloring of melasma can range from light brown to a blue-gray. Melasma can be categorized as epidermal, dermal, or mixed. Dermal melasma is characterized by melanophages. Epidermal melasma displays as an increase in melanin throughout the layers of the epidermis. Hyperpigmentation in the epidermis involves an increase in melanosomes and transfer of the number of melanosomes to the keratinocytes. Melanocytes become enlarged and have longer, thicker dendrites.

Melasma is complicated by its sensitivity to ultraviolet light. Expression of endothelial growth factor can lead to blood vessel changes such as telangiectasia and an inflammatory component. Solar elastosis is common in those with melasma. A lifetime subscription to sunscreen is essential, even if the condition has improved or completely disappeared. Melasma is known for its ability to chronically reoccur.

Melasma can affect all Fitzpatrick types, but most clients who present with melasma are type III and IV. In darker Fitzpatrick skin types, post-inflammatory hyperpigmentation may further complicate the treatment of melasma. The severity and distribution of melasma is measured by the melasma area and severity index (MASI).

The client consultation will provide clues to the cause of melasma. Treating mixed melasma can be tricky and setting client expectations is important. However, mixed melasma is still worth treating. Addressing epidermal melasma will even pigment and tone and possibly prevent more free melanin from cascading into the dermis and increasing dermal pigmentation. Dermal melasma is not reachable with lightening ingredients. Treating melasma while the hormonal component is still an issue will result in a longer treatment protocol and delayed results. In some instances, after hormones have stabilized, melasma may completely disappear without intervention.

THE UNUSAL SUSPECTS

For the past several decades, hydroquinone has and still is considered by many the benchmark treatment for hyperpigmentation despite some cytotoxicity concerns. Hydroquinone is a tyrosinase inhibitor. Tyrosinase inhibitors interrupt the process of melanogenesis early on. Natural alternatives to hydroquinone, like arbutin from bearberries and pear or cranberry extract have been a go-to alternative.

Tyrosinase is a copper dependent enzyme, so some tyrosinase inhibitors target copper by chelating it. If copper is taken out of the equation, then tyrosinase becomes ineffective.

While tyrosinase inhibitors are still popular, they are not the only method of interrupting melanogenesis or the distribution of melanin pigment. Niacinamide (vitamin B3) has become a popular choice for the treatment of hyperpigmentation. Topically applied niacinamide inhibits the transfer of melanosomes to keratinocytes. It also has anti-inflammatory properties.

Undecylenoyl phenylalanine is an amino acid unlike the usual tyrosinase inhibitor. In the process of melanogenesis, melanocyte-stimulating hormone binds to the melanocortin I receptor (MC1R). Undecylenoyl phenylalanine prevents the binding of melanocyte stimulating hormone to its receptor and in the process inhibits melanogenesis.[4] This is known as a melanocyte-stimulating hormone antagonist. Studies have shown the effectiveness of undercylenoyl phenylalanine on melasma and solar lentigines. Studies have also been performed on different mediums and their effectiveness in transporting undecylenoyl phenylalanine to where it is most efficacious. Research is ongoing with this treatment for hyperpigmentation.

"STUDIES AND RESEARCH INTO HYPERPIGMENTATION INGREDIENTS ARE OFTEN FOCUSED ON MULTIPLE INGREDIENTS THAT WORK SYNERGISTICALLY FOR AN OVERALL RESULT, INCLUDING CONTROLLED LIGHTENING OR BRIGHTENING, ANTI-INFLAMMATORY, ANTIOXIDANT, AND PHOTOPROTECTIVE INGREDIENTS."

AN ORAL OUTLOOK

Methimazole is an oral medication used to treat hyperthyroidism. Methimazole has been used for its depigmentation benefits when applied topically for melasma and post-inflammatory hyperpigmentation. In a study of 20 subjects with epidermal melasma, 5% methimazole was applied topically with few side effects. A study recommended that methimazole should only be applied to the areas of pigmentation.[7]

Rich in polyphenols, an extract known as polypodium leuctomos, is found in a tropical fern species. Taken orally, polypodium leuctomos has been studied as a possible addition to the topical treatment list for hyperpigmentation. In one study, participants were randomly selected to either receive 240 milligrams of oral polypodium leuctomos twice daily or a placebo over a 12-week period. The active and placebo groups were also treated daily with 4% hydroquinone and a broad-spectrum sunscreen. The results of the study indicated a greater reduction in the melasma area and severity index scores after 56 and 84 days of treatment in those taking polypodium leuctomos.

Tranexamic acid has been used orally for the treatment of melasma. Dosing is around 250 milligrams twice daily over a three-month period initially. It is not generally a first line treatment in the oral form. Tranexamic acid has also been used topically and with microneedling. It reduces melanin synthesis through various actions. Tranexamic acid also decreases mast cell activity and angiogenesis, both factors prevalent in melasma.

Hyperpigmentation is a concern for many clients and a condition that they will be looking for guidance and treatment on. As skin care professionals, it is important to be aware of the options available now and in the future. Research is ongoing and new ingredients are emerging. Not all the options for hyperpigmentation treatment are available under the scope of a professional license; the type of practice setting will determine the options available to the professional and their clients.

EMERGING ENTITIES

4-(1-phenylethyl)-1,3-benzenediol, or phenylethyl resorcinol exists naturally in scotch pine trees. It is considered a powerful tyrosinase inhibitor but not without its drawbacks. Studies have demonstrated a tendency towards contact dermatitis. Finding suitable carriers for this lightening ingredient may be key to its effectiveness in the future. More research is needed before it becomes a mainstream treatment for hyperpigmentation.

Piperlongumine, naturally sourced from the fruit of the long pepper (Piper longum), is being studied as a possible treatment for hyperpigmentation. Studies so far show promise as a tyrosinase inhibitor, as it inhibits tyrosinase-related protein I, tyrosinase-related protein II (dopachrome-tautomerase), and melanocyte-inducing transcription factor at various stages of the melanogenesis pathway.

Ellagic acid found naturally in fruits such as pomegranate, blackberries, strawberries, raspberries, and walnuts is emerging as a skin lightening agent. Several studies have been conducted on its effectiveness, demonstrating it may be more effective than arbutin. Like many lightening agents, ellagic acid is a tyrosinase inhibitor. Additionally, ellagic acid is considered a potent antioxidant.

Embilica officinalis, native to India (Indian gooseberry) has shown to inhibit tyrosinase and its related proteins tyrosinase-related protein I and tyrosinase-related protein II (dopachrome-tautomerase) through multiple stages of the melanogenesis pathway. In addition, Indian gooseberry is rich in vitamin C and offers blue light protection, making Embilica officinalis a possible treatment for hyperpigmentation. Studies have been done on this antioxidant rich fruit; perhaps it will become another ingredient that becomes mainstream in the treatment of melasma and other hyperpigmentation disorders.

Yet another ingredient that may emerge as an option for the treatment of hyperpigmentation is calycosin, a tyrosinase inhibitor. It is extracted from the root of the astragalus plant, part of the legume family, and native to China, Mongolia, and Korea.

Flutamide is an antiandrogen used topically at 1%. Studies are ongoing regarding its safety and efficacy in the treatment of melasma and other forms of hyperpigmentation.

Studies and research into hyperpigmentation ingredients are often focused on multiple ingredients that work synergistically for an overall result, including controlled lightening or brightening, anti-inflammatory, antioxidant, and photoprotective ingredients. Formulations and treatment protocols may consist of much more than one lightening or brightening ingredient in the continuous fight against hyperpigmentation so creativity is key.

With the three key criteria for the treatment of hyperpigmentation being lightening or brightening agents, exfoliation or cell renewal, and ultraviolet protection, clients and skin care professionals have options in their approach to hyperpigmentation remediation and treatment. The type of hyperpigmentation, whether melasma, post-inflammatory hyperpigmentation, or ultraviolet exposure will determine the best treatment options, taking into consideration the needs of the client and their ability to stick to a skin regimen. Safety and efficacy are key. A multitherapy approach to hyperpigmentation is required for obtaining the best treatment outcomes. d

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Kirsten Sheridan has a higher national diploma in beauty therapy from the United Kingdom and is a licensed aesthetician. She has 20 years of experience as an aesthetician and educator, holds a teaching qualification through City and Guilds London, and is a CIDESCO diplomat. Sheridan's other qualifications include massage therapy, aromatherapy, reflexology, and electrology. She has a personal training qualification through the National Academy of Sports Medicine (NASM), although not in active practice. In addition, she is the owner and founder of knowskin.com, an online learning hub for aestheticians and a DERMASCOPE Ambassador. Sheridan taught for Dermalogica, Illinois Dermatology Institute, San Francisco Institute of Esthetics and Cosmetology, San Jose City College, and The Dermal Sciences Institute.

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