Two forms of melanin are produced in the epidermis: phenomelanin, which is red to yellow in color, and eumelanin which is dark brown to black. The relative proportions of these also influence skin color. In addition, individuals differ in the number and size of melanin particles.

Skin pigmentation is influenced by several factors like:

- Hemoglobin in the blood vessels
- Carotenoids in the dermis
- Particularly, the dark pigment, melanin in the epidermis.

Production of Melanin

Melanin biosynthesis (melanogenesis) is influenced by genetics, environmental factors, diet and medication. The production of melanin by specialized cells called melanocytes (in the basal layer of the epidermis in light skinned people and in the basal as well as horny layer in dark skinned people) occurs through the action of the enzyme tyrosinase. The rate-limiting step in melanogenesis is the conversion of L-tyrosinase to melanin, through the action of tyrosinase. Copper and oxygen act as catalysts. Other enzymes also control melanin production, particularly in the presence of sulfur. These include the following:

- Dopachrome oxidoreductase which controls melanogenesis in the absence of tyrosinase. It helps to convert dopachrome into 5, 6-dihydroxyindole.
- Alpha-glutamyl transpepsidase which helps to maintain the balance in the biosynthesis of eumelanin and pheomelanin.

Variation in skin pigmentation is attributed to the levels of melanin produced and the number of melanocytes present. Although light skinned and dark skinned people may have the same number of melanocytes present, the rate of melanin production is greater in darker skin tones. Additionally, the melanin present in the epidermal layers of darker skins is resistant to enzymatic degradation. Increased production of melanin on one side of the skin and dramatically reduced decomposition of melanin on the other side results in darker skin tones, in light skinned people.

Melanin granules synthesized in the melanocytes are then transferred from the cytoplasm of the melanocytes to the basal cytoplasm of the keratinocytes. They thus form a protective covering in the inner layers of the epidermis, absorbing UV rays and inhibiting their penetration.

Controlling Melanin Synthesis

Various types of inflammatory mediators such as leukotrienes and prostaglandins, cytokines and growth factors may influence melanin synthesis by affecting the proliferation and functioning of melanocytes. This explains why inflammatory diseases often induce hypopigmentation or hyperpigmentation. The enzyme, protein kinase C that phosphorylates proteins may also influence the growth and differentiation of melanocytes. Cytokines such as endothelins (also known as vasoconstrictive peptides) are also reported to accelerate melanogenesis.

Quick view of our Main Products

- **TetraPure and Sabiwhite** (tetrahydrocurcuminoids) : anti-tyrosinase activity along with High ORAC value, and Inhibition of Melanogenesis
- **Glabridine** (from 4% to 98% from licorice): the well-known whitening agent
- **pTeroWhite®**:new studies on pterostilbene purified from Pterocarpus marsupium
- **Saberry** (β-glucogallin from Amla) : white water soluble Skin Whitening, MMP-1 Inhibitor, UV Protector
- **OxyResveratrol Artonox**: strong and dose dependent inhibition of Tyrosinase enzyme activity and melanogenesis inhibitory activity
- **Ellagic Acid** (pomegranate), lightening, UV protection, also in oral form
- **Fucoxanthine** (wakame) : lessened UVB-induced epidermal hypertrophy, VEGF, and MMP-13 expression
- **Soy extract** : lightening action in solar lentigenes (hyperpigmentation due to sun)

Skin lightening cosmeceuticals

The toxicity associated with hydroquinone use, induced researchers to identify less dangerous botanicals with comparable activity. The general modes of action include inhibition of the formation of melanosomes, inhibition of tyrosinase biosynthesis, and inhibition of melanin biosynthesis and interference of the transfer of melanosomes into the keratinocytes. Some agents also have a chemical effect on melanin with an increase in the degradation of melanosomes in the keratinocytes.

Antioxidants such as ascorbic acid and others help to decompose preformed melanin. Hyperpigmentation due to UVA and UVB damage may also be addressed by preventive measures using antioxidant compounds with sunscreen effect and free radical scavenging action. Research efforts are generally aimed at achieving one or more of the following effects:

- **Regulation/inhibition of tyrosinase**, dopachrome oxidoreductase and dopachrome tautomerase involved in melanogenesis
- **Regulation of cytokine** network including endothelin
- **Regulation of genes** related to melanogenesis
- **Combinations** of the above approaches

The concept of skin lightening is not limited to decreasing melanin in skin but also encircles age spots, Melasma, Chloasma, Freckles, Post inflammatory hyperpigmentation Sun induced pigmented blemishes.

pTeroWhite®

Two new studies recently published:

- An Open-Label Single-Arm, Monocentric Study Assessing the Efficacy and Safety of pTwroWhite® for Skin Brightening and Antiaging Effects: significant improvement in under-eye fine lines at all-time points and in wrinkles, frown lines, and crow's feet area at the end of the study. The pterostilbene preparation was able to improve the skin luminosity with continuous application.
- A second clinical study, a randomized study to determine the Sun Protection Factor of pTeroWhite® demonstrated the effect as a natural SPF ingredient, the potent antioxidant effects in various in vitro and cellular test systems, and the safety.

Artonox™

With Tetrapure® and Glabridin 98%, Artonox™ is a new comer in our range for skin brightening. Obtained from the dried wood of *Artocarpus lakoocha*, it provides 95% of Oxyresveratrol, an analog of Resveratrol (a stilbenol 2',3,4',5-tetrahydroxystilbene). Oxyresveratrol exhibits bout 150 fold more potent skin lightening inhibitory effect than Resveratrol (3,4',5-trihydroxystilbene), and 32 more than Kojic.

Artonox™ is dedicated for:

- Skin lightening formulations
- Antioxidant
- Anti-aging formulations

Skin Brightening

When Skin Needs Brightening

Optical properties modulate the appearance of skin. Skin needs brightening when:

- Too transparent or too highly pigmented skin appears spotted and unhealthy.
- When skin is dull. Dull skin is dehydrated skin which is to transparent or hyper pigmented.
- Early aged skin is also dull and rough due to loss of surface integrity.

What Skin Brightening Cosmeceuticals do

The effects of skin brighteners are:

- Radiant complexion.
- Beautiful skin glow.
- Even skin tone, without freckles, age spots or other types of discoloration.
- Rejuvenated, nourished and smooth skin

Other related products

Tyrosinase inhibitors such as Arbutin (from the leaves of the common bearberry), Arctophylos urva ursi and other plants, Glabridin from licorice (Glycyrrhiza glabra roots), ascorbic acid and its derivatives, Kojic acid (a bacterial carbohydrate metabolite) are better tolerated than hydroquinone. Aloesin from Aloe is reported to be a non-competitive inhibitor of

FOCUS HINTS

tyrosinase, affecting (...)(...) the action of tyrosinase complex in the substratum and reducing the conversion of DOPA into melanin.

Arbutin and Kojic acid inhibit tyrosinase directly, while L-ascorbic acid and its derivatives are believed to act as reducing agents on intermediates in melanin biosynthesis at various points in the oxidation chain reaction from tyrosine/DOPA to melanin. Our products are usually compared to Arbutin and to Kojic acid.

Green tea is also reported to be a competitive tyrosinase inhibitor through the gallocatechin moiety in the major catechin constituents epicatechin gallate, epigallocatechin gallate and gallocatechin gallate.

Paper mulberry extract (from the root bark of Broussonetia kazinoki x B. papyrifera) also contains active depigmenting agents, which were shown to be more efficacious than hydroquinone (IC 50 of 2.5 mg/ml against 5.5 mg/ml for hydroquinone).

Comparative table sheet	Orac	DPPH	Tyrosinase	Melanin	Elastase	Collagenase	UV Protection
Artonox	19 735	2,700	0,049	12,000	120,000	92,000	n.c.
Glabridine 40%	3 256	49,000	0,250	3,000	n.c.	n.c.	n.c.
Pterowhite	12 508	4,900	6,900	0,550	n.c.	n.c.	30
Resveratrol	25 223	3,010	5,500	2,500	n.c.	n.c.	31
Saberry	2 682	n.c.	321,000	14,000	n.c.	n.c.	15 [UVA] 42 [UVB]
Sabiwhite	10 786	n.c.	1,770	3,000	n.c.	n.c.	n.c.
Tetrapure	10 212	1,300	1,800	3,200	n.c.	n.c.	n.c.
Kojic Acid	-	500,000	7,000	100,000	n.c.	n.c.	n.c.
Vitamin C	3 400	1,930	9,330	25,000	n.c.	n.c.	n.c.
Arbutin	-	500,000	193,600	100,000	n.c.	n.c.	n.c.

- **ORAC Value** : µmol Trolox equivalents/g *(Higher is greater)*
- **DPPH Inhibition:** IC50µg/ml *(lower is greater)*
- **Tyrosinase Inhibition**: IC50µg/ml *(lower is greater)*
- **Melanin Inhibition**: IC50µg/ml *(lower is greater)*
- **Elastase Inhibition**: IC50µg/ml *(lower is greater)*
- **Collagenase Inhibition**: IC50µg/ml *(lower is greater)*
- **UV Protection**: IC50µg/ml *(lower is greater)*