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The **Dermamelan** method has been designed to attenuate/eliminate darkened skin spots of melanic origin.

This unaesthetic but frequent problem has different origins. Among them:

- Genetics
- Race
- Sex
- Pregnancy
- Oral contraceptives
- Menopause, etc.

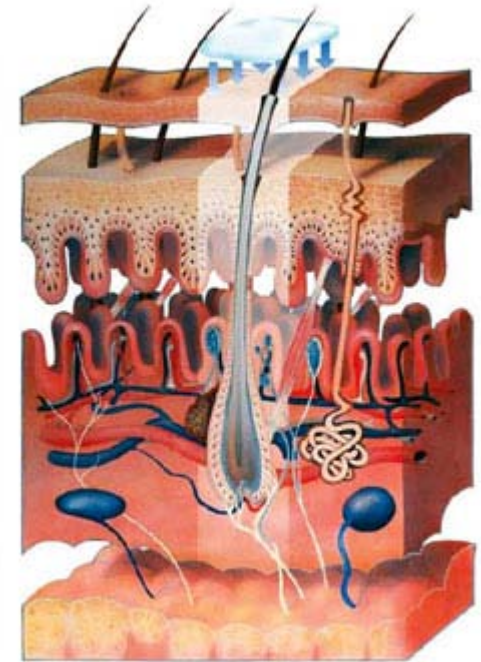
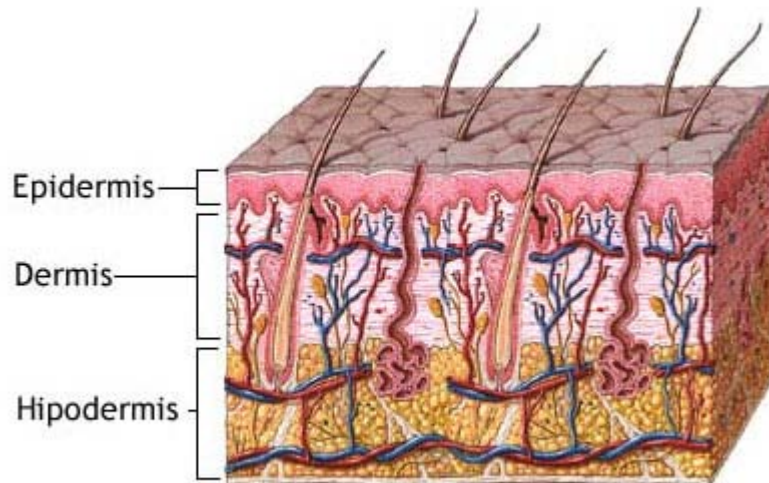
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The Dermamelan method works with the cells responsible for skin coloration stopping color production in areas where there is an excessive production and successfully achieving the:

**ELIMINATION or ATTENUATION OF
UNAESTHETIC SKIN SPOTS**

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SKIN STRUCTURE



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Skin structure and histology

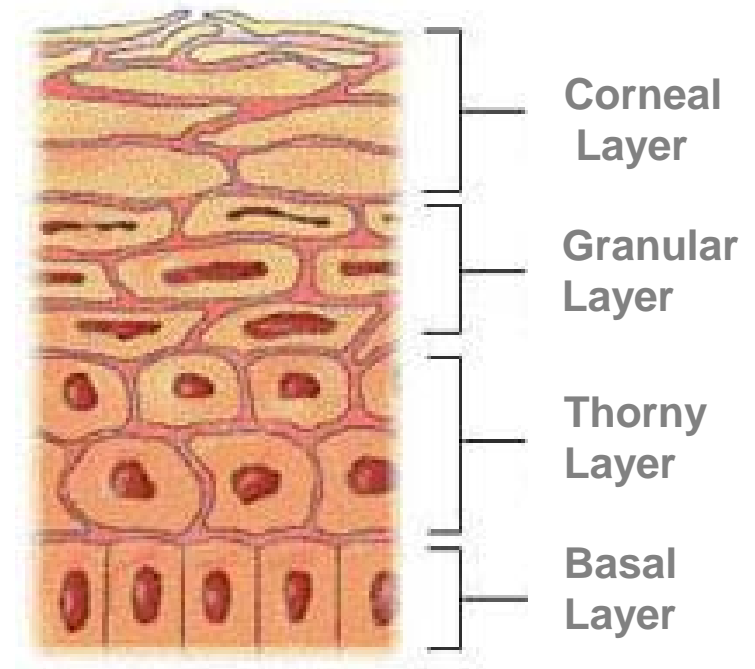
Epidermic cells:

- **Keratinocytes**
- **Langhergans cells**
- **Melanocytes**

Melanosomes: factory of melanin

Functional melanodermic unit:

1 melanocyte + 30/40 keratinocytes



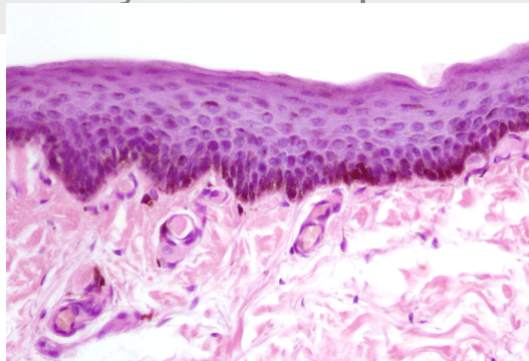
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Skin structure and histology

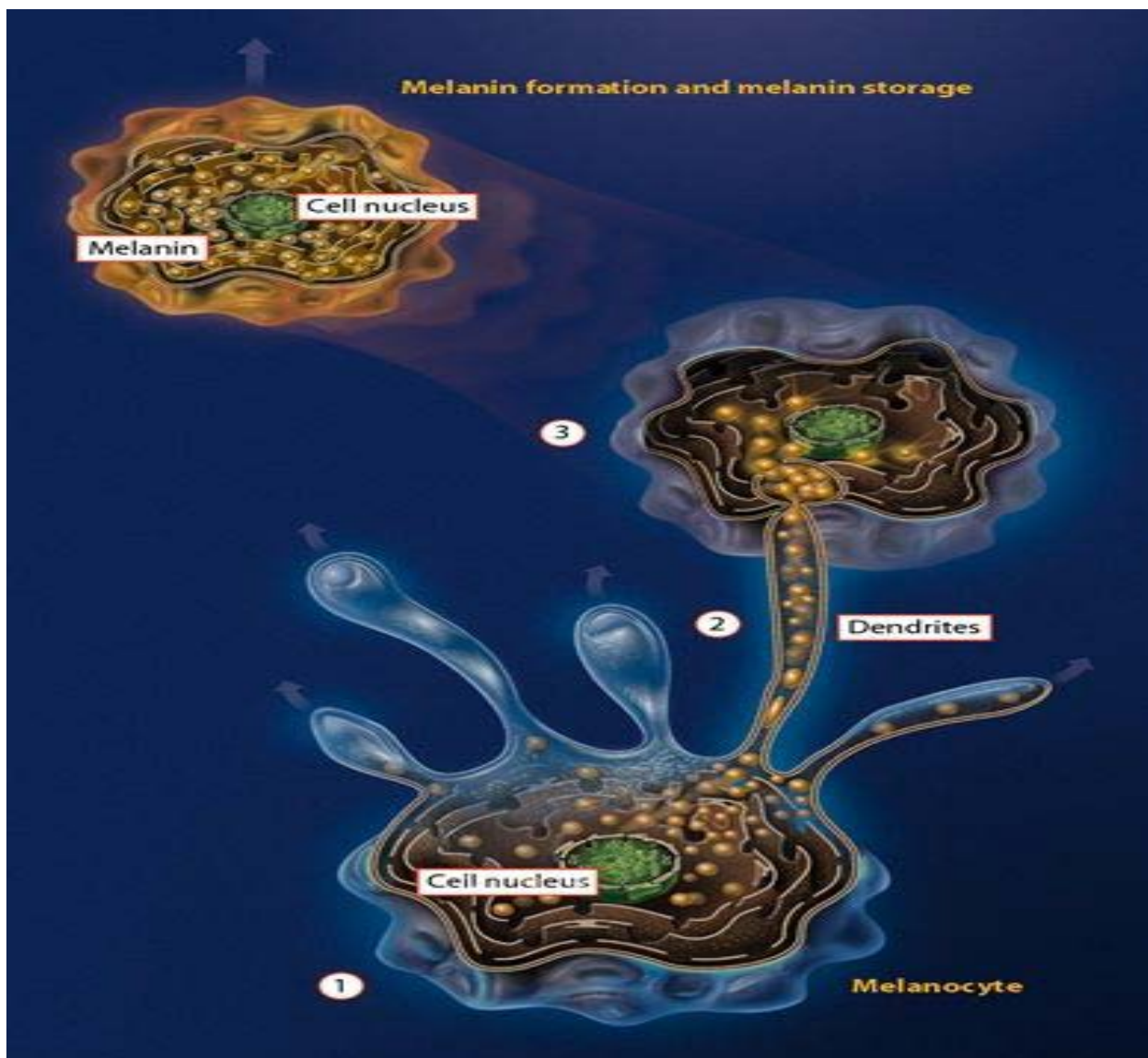
Through the dendritic branches of the melanocyte, the **melanosomes** containing melanin are injected into keratinocytes.

Keratinization: Proliferation & differentiation of the keratinocytes which lead its transformation into a corneocytes

Melanin remains inside the corneocytes. Those, appear conjointly with ceramids forming the corneal layer of the epidermis

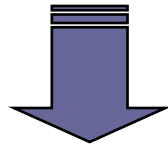


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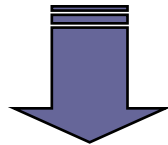


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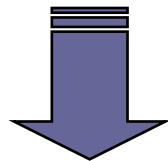
Melanogenesis in-
side melanosomes



Tyrosinase lack of
activity inside
melanosomes



Dendritic branches



Keratinocytes fagocytosis



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Common metabolic pathway in melanin's biosynthesis

Key step:

TYROSINE OXYDATION by TYROSINASE to produce DOPA (dihydroxyphenylalanin)

2^o step:

OXIDATION of DOPA to DOPAQUINONE by TIROSINASE.

3^o step:

Through an AUTO-OXIDATION process the DOPAQUINONE is converted to DOPACHROME

Two types of melanin depending on the genetic determination.

EUMELANINES



PHEOMELANINES

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EUMELANINES Metabolic pathway

DOPACHROMO turns in to:

DHI: dihydroindole.

DHICA: dihydroindole- 2 carboxylic acid

Through complex polymeration reactions above intermediate products, are converted in EUMELANINS.

Pigmentation of darker skin color people.

Excellent photo protection capacity.



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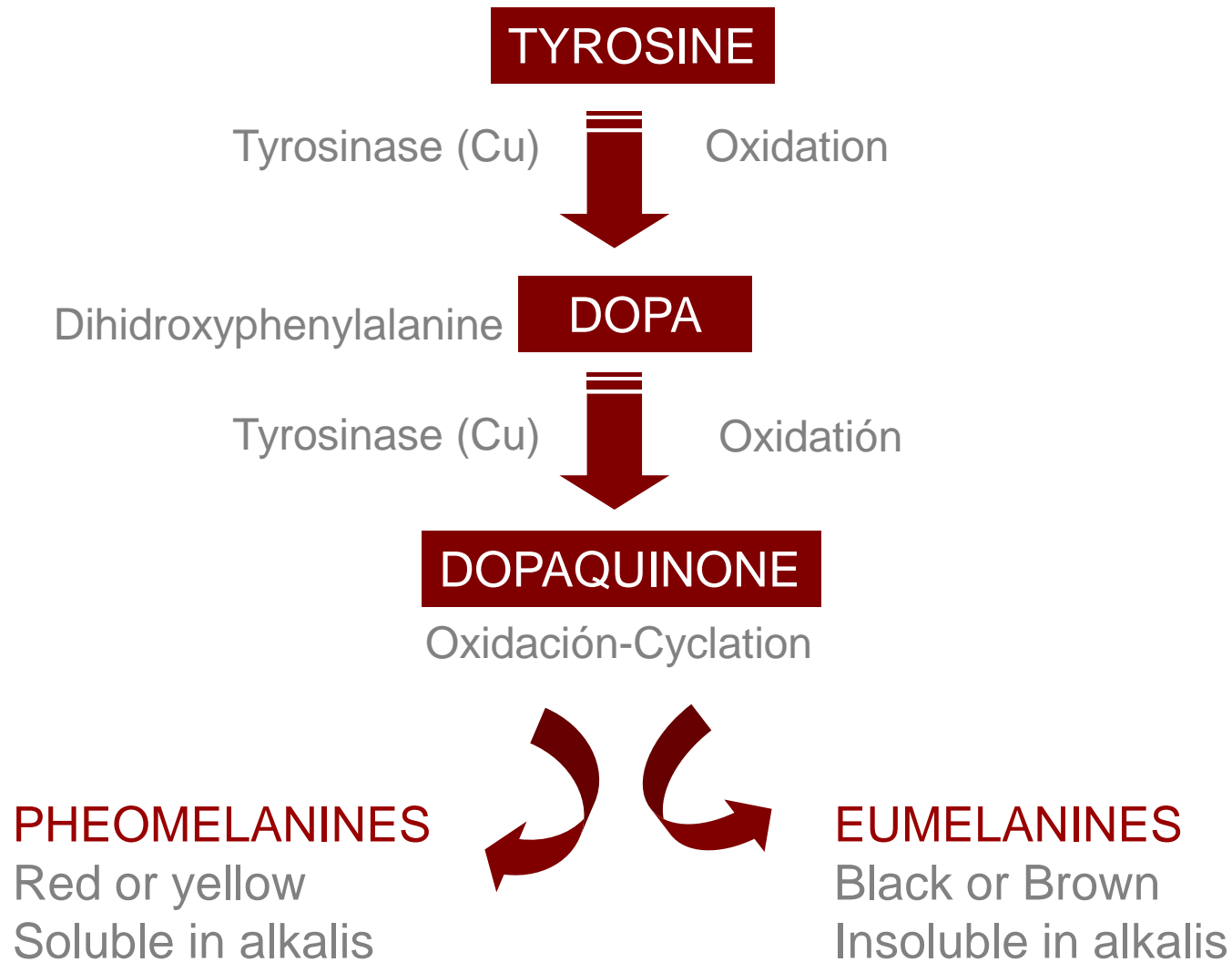
PHEOMELANINES Metabolic Pathway

With cysteine or glutathione, the DOPOAQUINONE is converted in:
Cysteinyl DOPA or,
Glutathione DOPA.

Through complex polymeration reactions above intermediate products, are converted in PHEOMELANINS.
Pigmentation of white & redhead people.
Scarce photoprotection capacity



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TIROSYNE

DOPA

DOPAQUINONE



Tyrosinase

Tyrosinase

Oxidation
Cyclation

DOPA

DOPAQUINONA

Eumelanine pheomelanie

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Blockage of the TYROSINASE & OXIDATION

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Melanogenesis: Melanin Synthesis

Melanin functions:

Protection mechanism of the skin

Responsible for skin, eyes and hair **color**

Protects against **photoaging & photocarcinogenesis**

Protects DNA from actinic injuries

High **chemically stability**



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Melanin synthesis regulation

The most important factors in melanogenesis are UV radiations (**UV-A & UV-B**)

An indirect stimulus could be an ADN fragment caused by UV rays aggression

Regulation of the melanogenesis is **local**, complex & little known mechanism related to **endocrine, paracrine & autocrine** process through several cytokines between keratinocytes & melanocytes.

The hormone involved in the regulation process is **alpha-MSH**, produced not only in the hypophysis but also in skin cells (autocrine & paracrine regulation).

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Melanin Synthesis

Important aspects in melanogenesis

TYROSINASE is the heart of all pathways

Coenzyme with important influence: COPPER, also playing a role (although less important): ZINC & IRON.

Substances blocking tyrosinase, can cause **HIPO**pigmentation. But some others, irritative ones can cause post inflammatory **HIPER**pigmentations.

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INMEDIATE stimulus of
the Melanogenesis :



By the **oxidation of the preformed melanin**

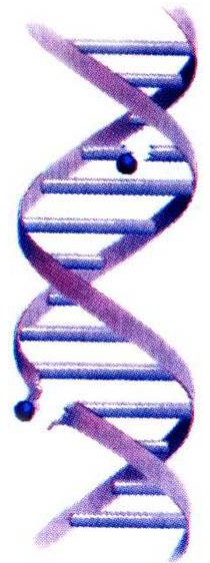
- UV-A rays
- Visible light

LATE stimulus of the
Melanogenesis



As a consequence of the new melanin synthesis caused by an inflammatory process

- UV-B rays



Main influencing factor:
Genetics & exposure to the UV rays

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DEPIGMENTATION METHOD



Natural physiologic way of melanin's elimination :

EXFOLIATION process of the corneocytes

Each day a part of the corneocytes in the corneal layer is lost and with it the melanin they carry.

This process may be accelerated or slowed down by several internal and external stimulus

Alternative way to eliminate melanin :

Macrophagic cells (monocytes), work to eliminate the abnormal location of melanins in dermal areas.

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HIPERPIGMENTATION

Increase of skin natural color

Darkened spots have two main causes

Acquired

Hyperplasia caused by hyperproduction of melanin by melanocytes.

Hypertrophy of the located melanocytes

Non acquired

Related with genetic or hereditary predisposition.



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Hyperactivity of melanocytes :

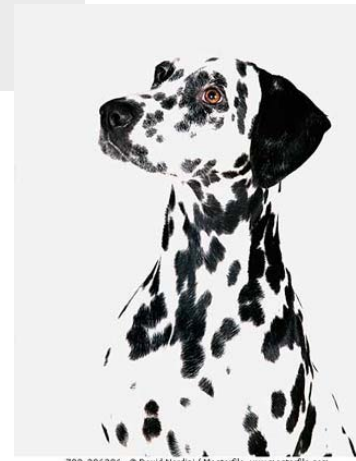
Melasma y cloasmas

Located melanocytes produce Eumelanins instead of Pheomelanins. Phototypes I,II,III

Freckles

Normal melanocytes producing an excess of melanins.

They are stimulated by sun radiation.
Occurs in fair skins.



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Melanocytes hyperproliferation

Lentiges (actinic & aging)

Phototoxicity

Post inflammatory process

Mechanical, physical, or chemical injuries which evoke an inflammatory state after leading to skin hyperpigmentation (acne, laser, peelings, wounds...)



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HYPERPIGMENTATION DIAGNOSTIC

Determining the cause of hyperpigmentation is important to select the best approach for the treatment

Patient's clinical record

Hyperpigmentation etiology

Wood Light Exam. This light emits radiations close to the highest absorption of melanin.



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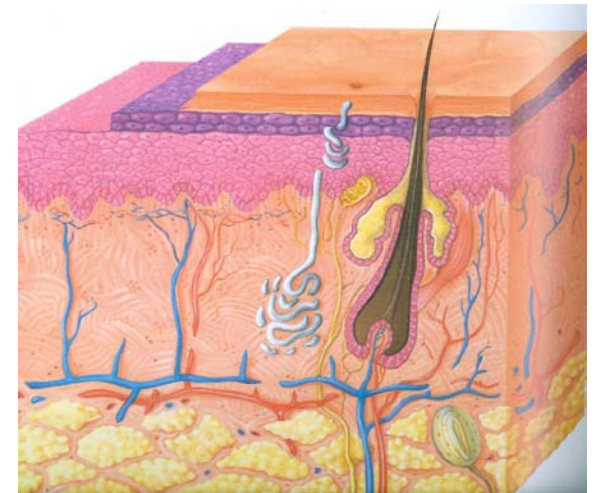
Spots are classified according to its localization

Epidermic

Dermic

Mixed

Non visible



Depigmentation products strategy

Remove darkened spots

Skin lighten

Skin embellishment, improve its look



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Depigmentation mechanisms

Inhibition of the enzymatic process involved in the melanogenesis: **Tyrosinase** & other oxidases

The enzymatic inhibition is **REVERSIBLE**

The target is the **melanosome**

Lightening agents do not operate on melanin spots. Its elimination depends on **natural mechanisms of melanin clearance** (skin exfoliation, phagocytosis by macrophages & skin cells).

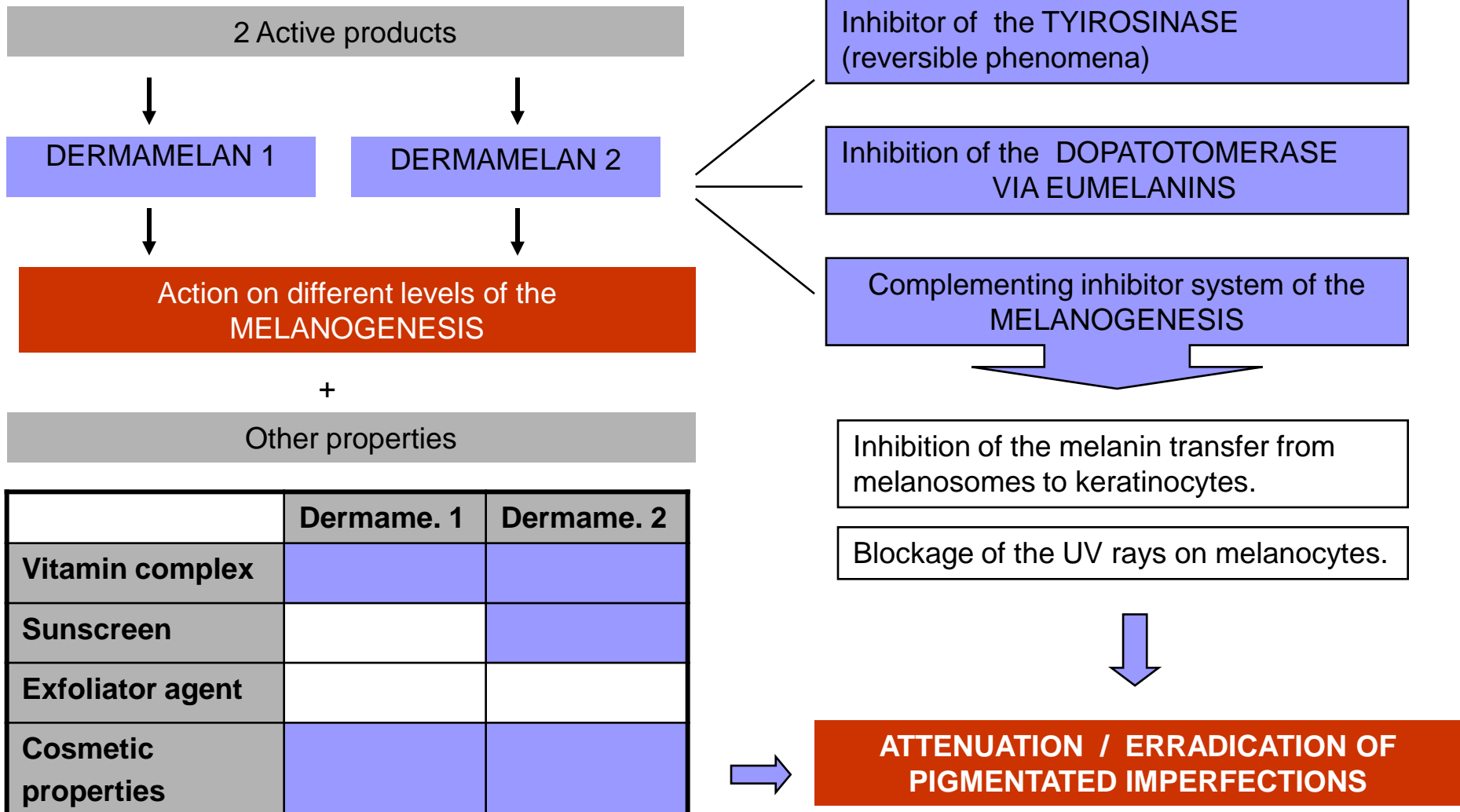


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DERMAMELAN 1 y 2 Depigmentation topic treatment



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2 cycles

Cycle 1: CORRECTION
OF IMPERFECTIONS

Cycle 2: MAINTENANCE

1/ Degreasing solution

+

2/ DERMAMELAN 1 Application

Home application DERMAMELAN 2

3-2-1 Method



1st month: application 3 times per day

2nd-3rd month: application 2 times per day

From 3rd to 9th month: 1 application night

+

**OBLIGATION:
SUNSCREEN**

Complete moisturizing &/or
Dermatologic **sunscreen**

For occasional blemishes
MELANOGELO TOUCH

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Vs



Same qualitative composition in functional cosmetic ingredients

Variable quantity. Higher amount of substances in COSMELAN TREATMENT

This higher concentration creates an **increased gradient of depigmenting agents** in the corneal layer

Highly Effective concentration of depigmenting agents inside melanosomes

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Functional composition

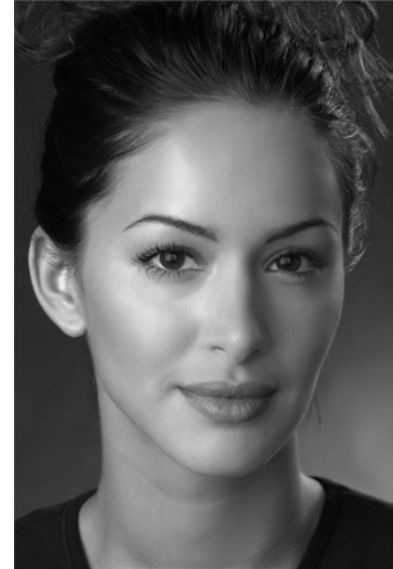
SUN FILTERS (SPF) = UVB/A+++

Non cytotoxic REVERSIBLE Tyrosinase inhibitor

Skin embellisher agents

Penetration enhancer of other active ingredients

Melanin removal accelerator



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SUN SCREENS: Eliminate UV stimulus

Organic

Protection against UVB radiation (290-320 nm)

Protection against UVA radiation (320-400 nm)

Inorganic

Protection against UVA-UVB (290-400 nm).

It adds a new filter, non whitening, with a wide capacity to protect against UVA-UVB. It does not generate free radicals and improves the stability of organic filters

[Sun screen SPF 20 Anti A : +++]

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INGREDIENTS	INHIB. TYROSINASE	OTHER EFFECTS	ENHANCES PERMEABILITY	EMBELLISHES SKIN	ACCELERATES ELIMINACIÓN
AZELAIC ACID					
KÓJIC ACID					
ALFA ARBUTINE					
RUMEX LANA					
TIROSINOL COMPLEX					
ALOE BARBADENSIS					
CYNAMON EXTRACT					
ASCORBIC PHOSPHATE					
NIACINAMIDE					
AMINOETHILPHOSFÍNIC ACID					
NONAPÉPTIDE-1					
RETINOL					
TOCOPHEROL					
ASCÓRBIC ACID					
BISABOLOL					
ETHOXIDIGLICOL					
SALICYLIC ACID					

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Tyrosinase Inhibitors non cytotoxic

Azelaic acid : Bacteriostatic against aerobics. Competitive inhibitor of 5-alpha-reductase. It reduces sebum secretion

Kojic acid: quelant and antioxidant. Bacteriostatic

Alpha-Arbutine: Biotechnological origin. It's stronger than beta arbutine (natural origin)

Rumex extract: Anti-erythematic

Tyrosinol

Aloe barbadensis (aloesin).

Licorice extract: anti-inflammatory and demulcent

Ascorbic acid: Antioxidant skin whitening

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OTHER FEATURES AGAINST MELANOGENESIS

Azelaic: Reduces melanocytic hyperplasia

Niacine: Decreases melanosome transfer from melanocytes to keratinocytes

Ethyl fosfonic acid: dopa tauomerase inhibitor

Tyrosinol: enzyme inhibitor of TPR 1 and TRP 2

Nonapeptide-1: alphaa – MSH receptor inhibitor

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EMBELLISHERS AND ANTIAGING

Retinol: Stimulates epidermic kinetic. Antioxidant. Prevents from wrinkle formation.

Tocoferol: Antioxidant. Protects cellular membranes from peroxidation. Avoids collagen crosslink and protein glycation.

Ascorbic acid. Stimulates fibroblastic functions. Antioxidant. Neutralizes free radicals

Aloe Barbadensis: Moisturizing, revitalizer, healing

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SKIN PERMEABILITY MODIFIATORS:

Increase permeability of depigmentation ingredients into the corneal layer

Bisabolol

Etoxidiglicol

PROMOTER OF MELANIN ELIMINATION

Salicylic acid: Accelerates corneocyte and keratinocyte kinetics

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Topic depigmentation strategies

Utilization of depigmentators has the following finalities:

Eliminated non-wanted melanin accumulation

- To bleach the skin
- To embellish the skin

Depigmentation mechanism:

Every topic depigmentator acts inhibiting, reversibly, the enzymatic mechanism of melanogenesis.

The key enzyme is tyrosinase, although there are others participating.

Enzymatic inhibition is reversible.

Topic depigmentator does not act directly on the melanic spot. Its elimination depends on the physiologic elimination mechanism, which can be stimulated (exfoliation)

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Topic depigmentation strategies

Spot elimination takes time (weeks or months) due to the process.

Depigmentants arrive to melanosomes by diffusion in the corneal layer, usually highly impermeable

The negative effect of UV light must be abolished to get good results (sunscreen)

Since enzymatic inhibition is reversible, depigmentation application should be frequent during a long period.

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Results



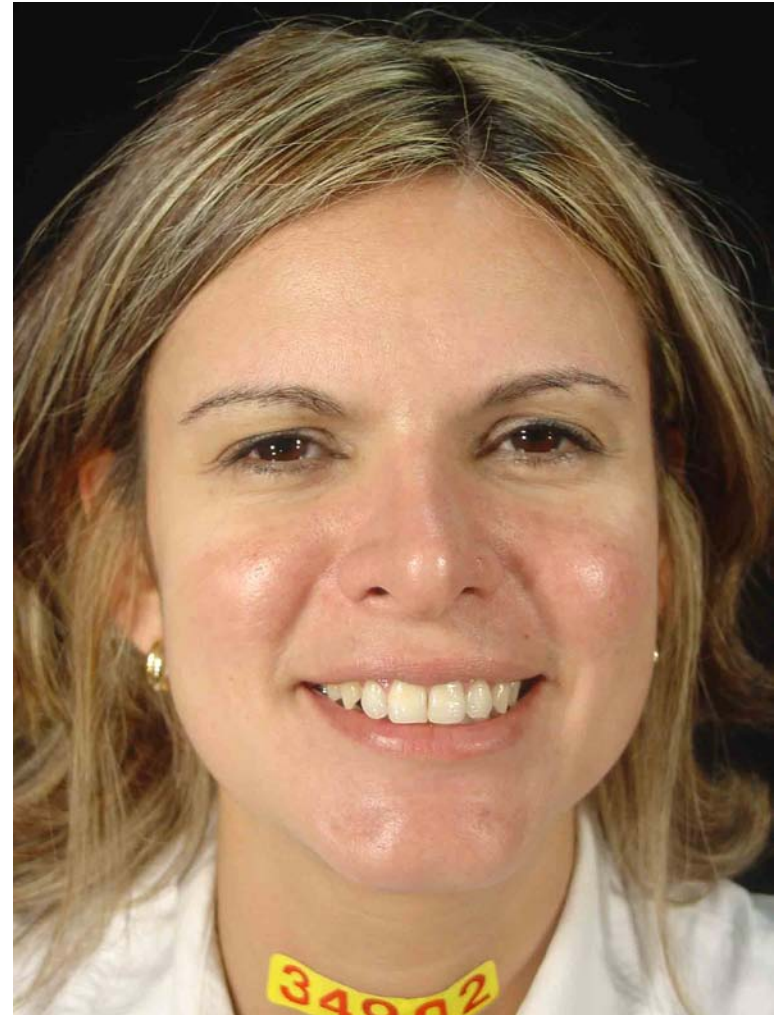
Significant **attenuation, decrease or disappearance of melanic spots** at the third or fourth week of treatment

Renovation and embellishment of the skin at the second week of treatment

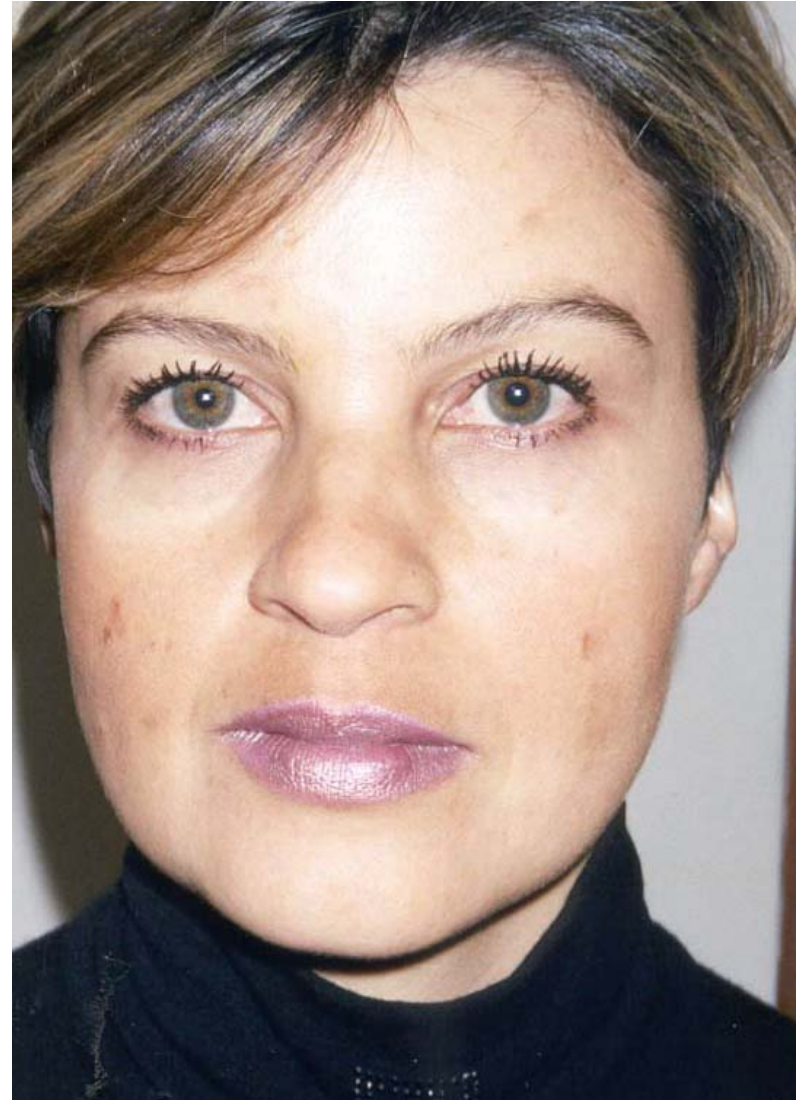
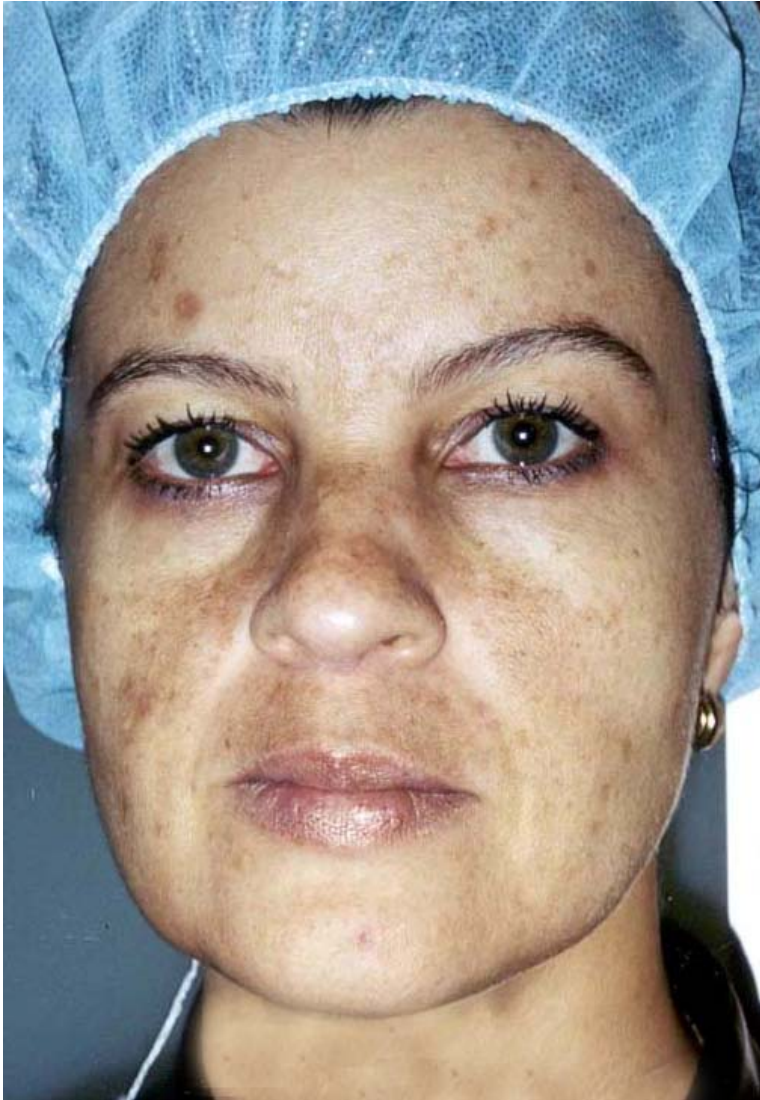
Stimulation of capillary circulation and neoangiogenesis

Rosy and bright skin effect

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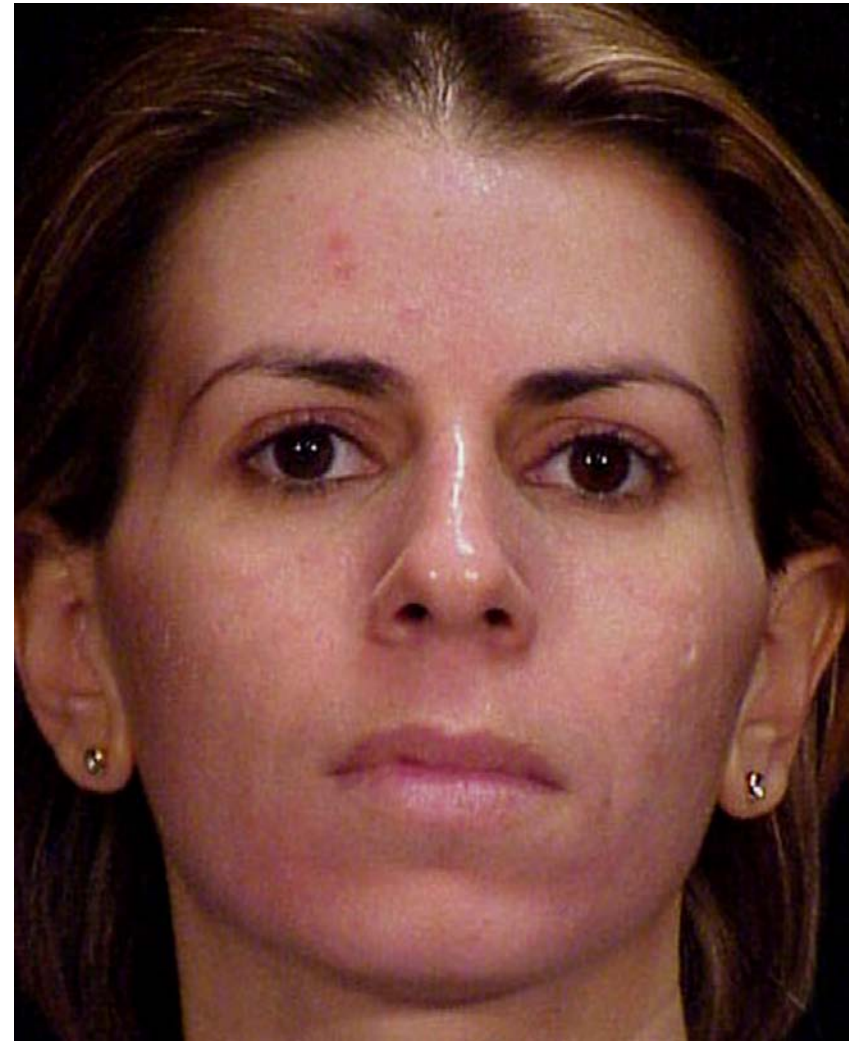
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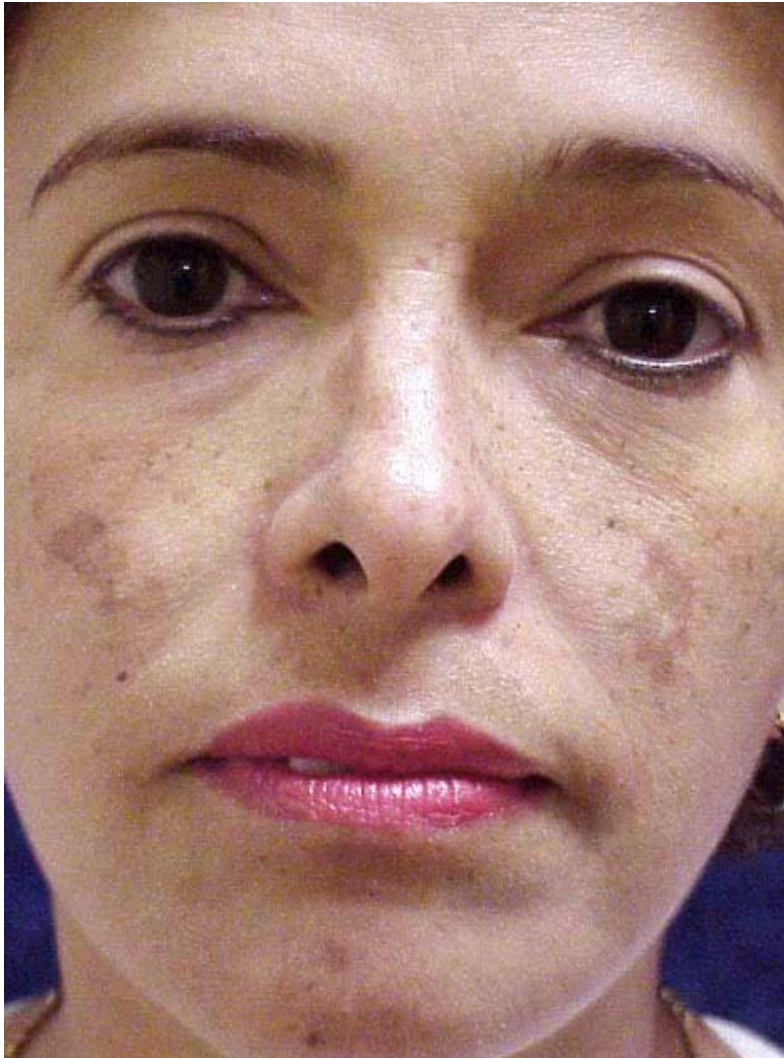
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Thank you for your attention



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