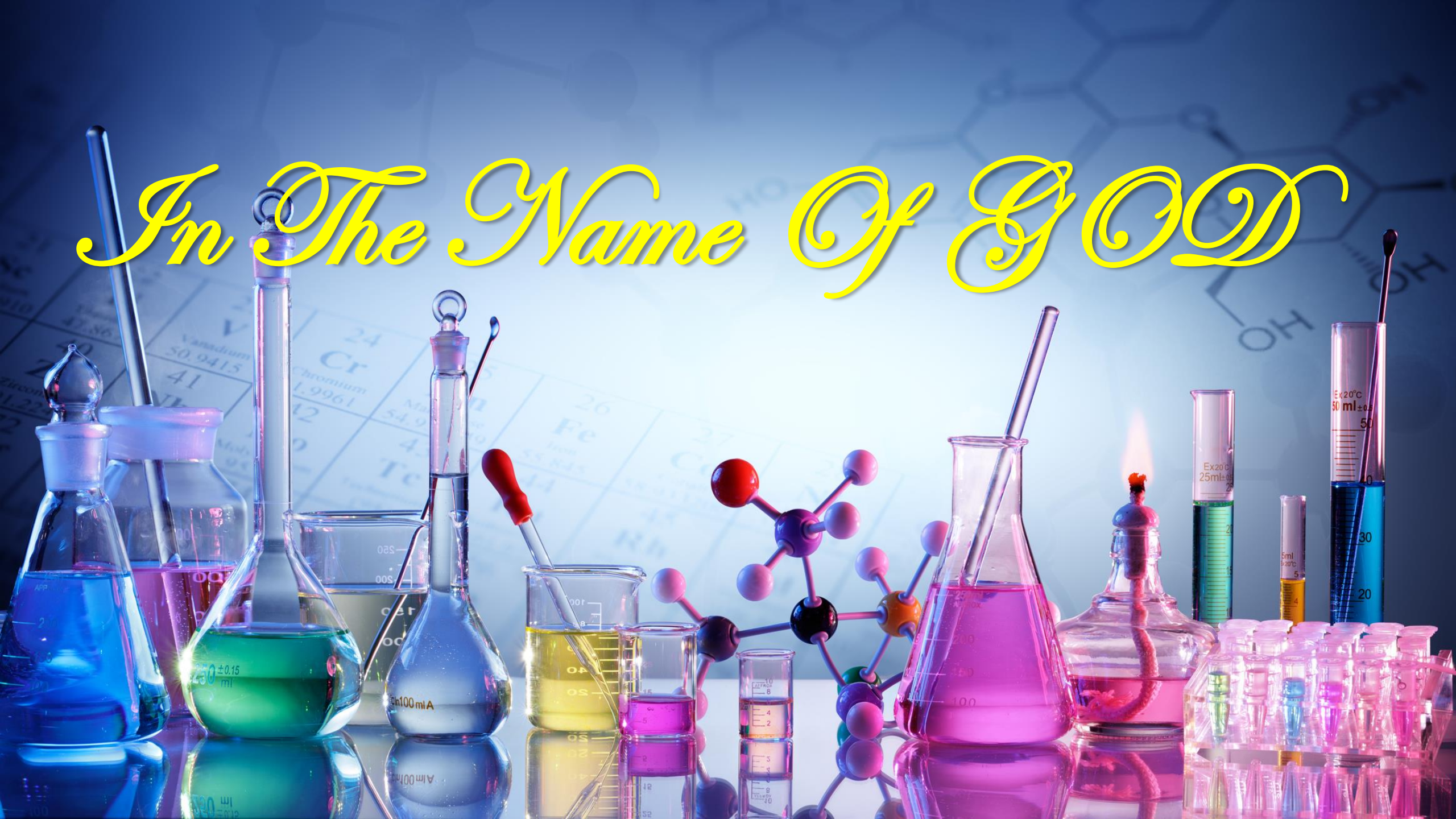
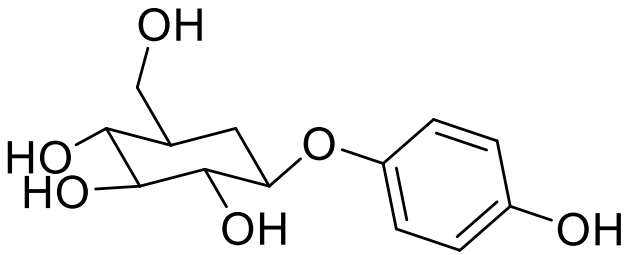
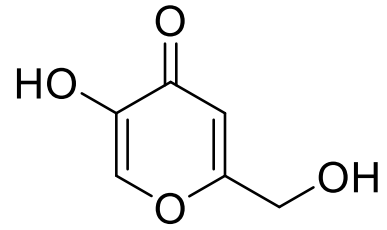
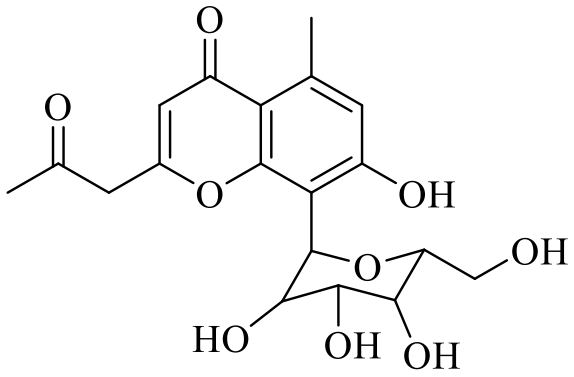

In The Name Of GOD

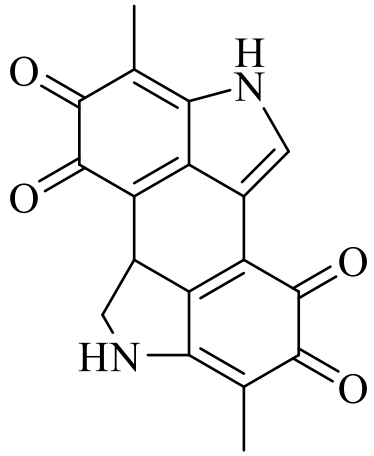
Tyrosinase Inhibitors as Skin-lightening Agents

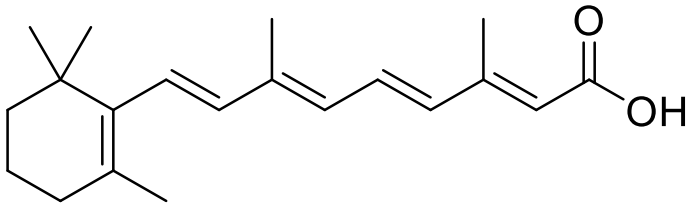




Presented By
Dr. Somaye Karimian







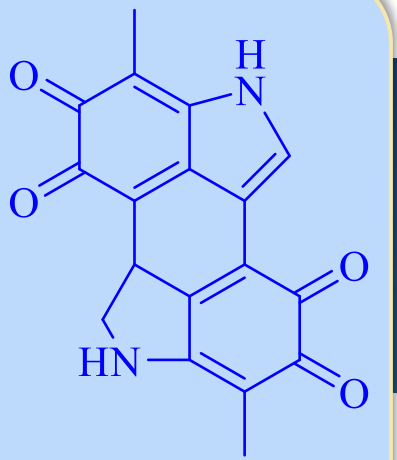
1402/08/29
2023 November

Skin-lightening Agents

- The global market for Skin Lighteners estimated at US$8.8 Billion in the year 2022, is projected to reach a revised size of US$11.8 Billion by 2026.

- https://www.prnewswire.com/news-releases/valued-to-be-11-8-billion-by-2026--skin-lighteners-slated-for-robust-growth-worldwide-301488228.html

Melanin



Melanin

- **Melanin** is a broad term for natural pigments found in most organisms. It is a complex polymer derived from the amino acid tyrosine. Melanin pigments are produced by melanocytes, specialized cells that determine the distinct color of your eyes, hair, and skin.

Melanin

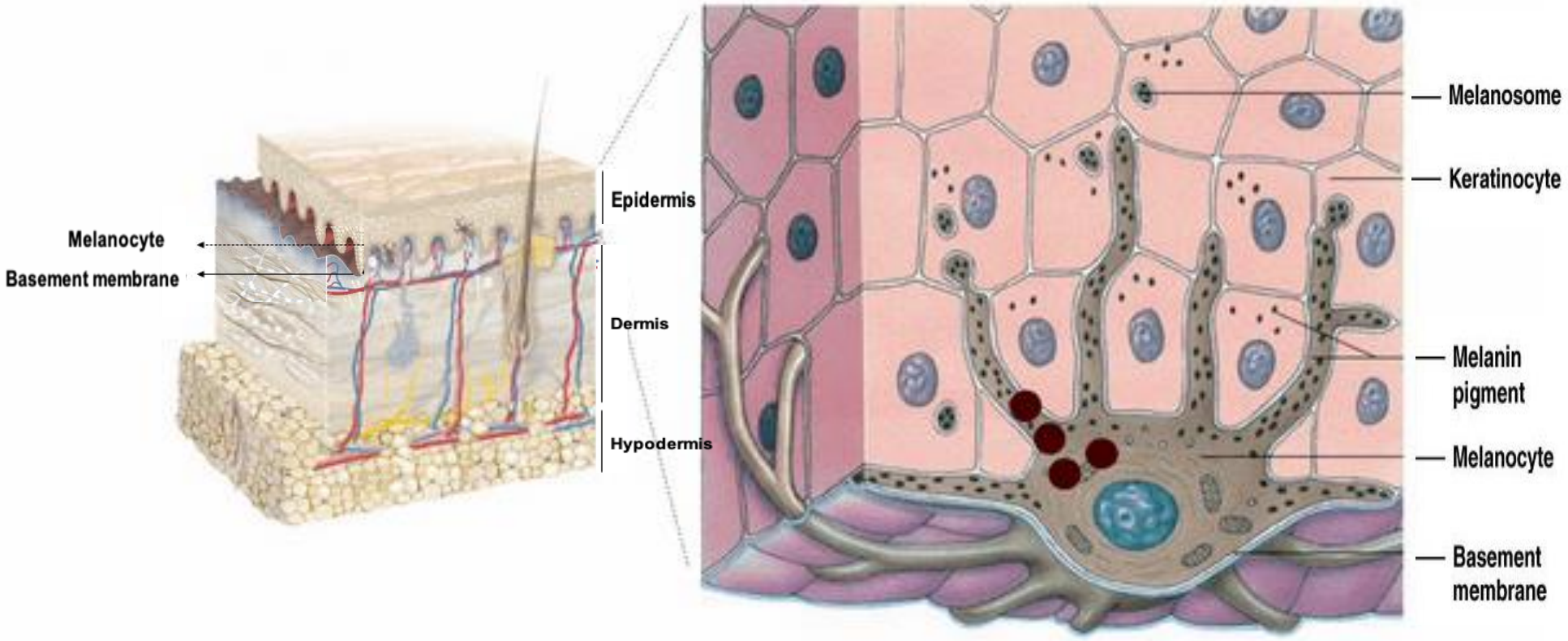
➢ **Where is melanin in your body?**

The cells that make melanin can be found in different parts of your body, including:

- The deepest layer of skin
- Parts of eye, including the pupil and the iris
- hair
- Part of inner ear
- Areas of brain and adrenal glands

Melanogenesis

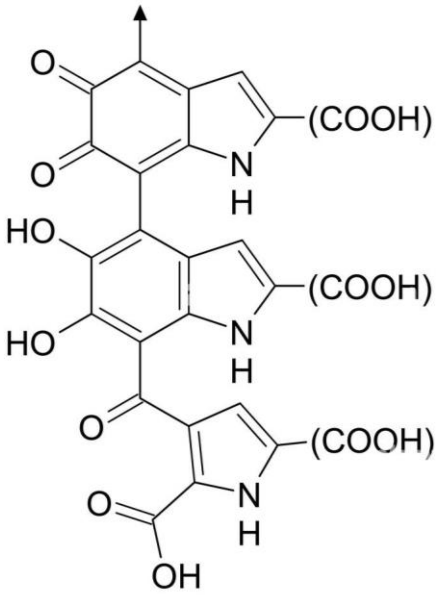
Melanocytes produce melanin in the so-called basal layer, which is the innermost layer of the epidermis. Keratinocytes then carry melanin to the skin surface.



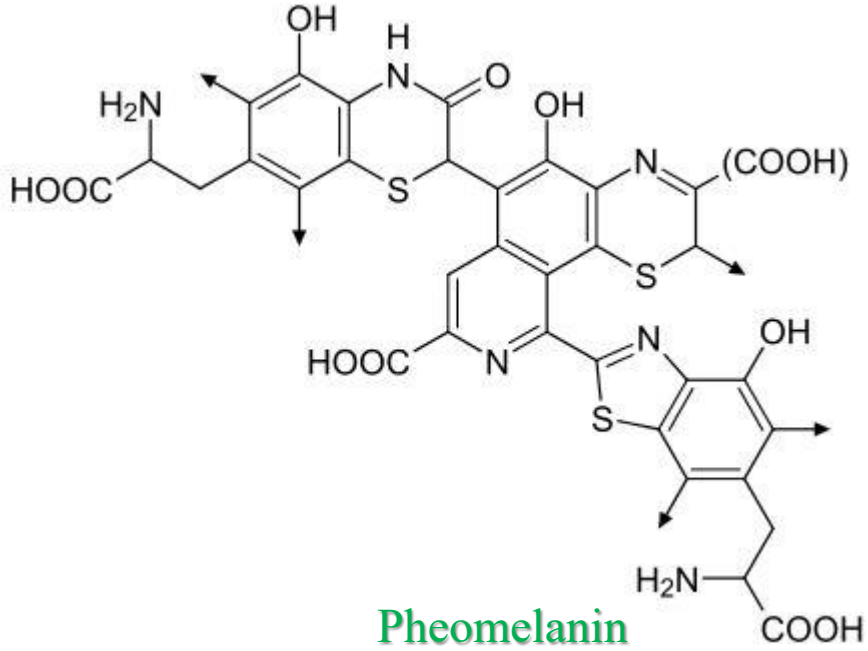
Types of Melanin

➢ There are five basic types of melanin:

- Eumelanin
- Pheomelanin
- Neuromelanin
- Allomelanin
- Pyomelanin



Eumelanin



Pheomelanin

Melanin and skin disorders

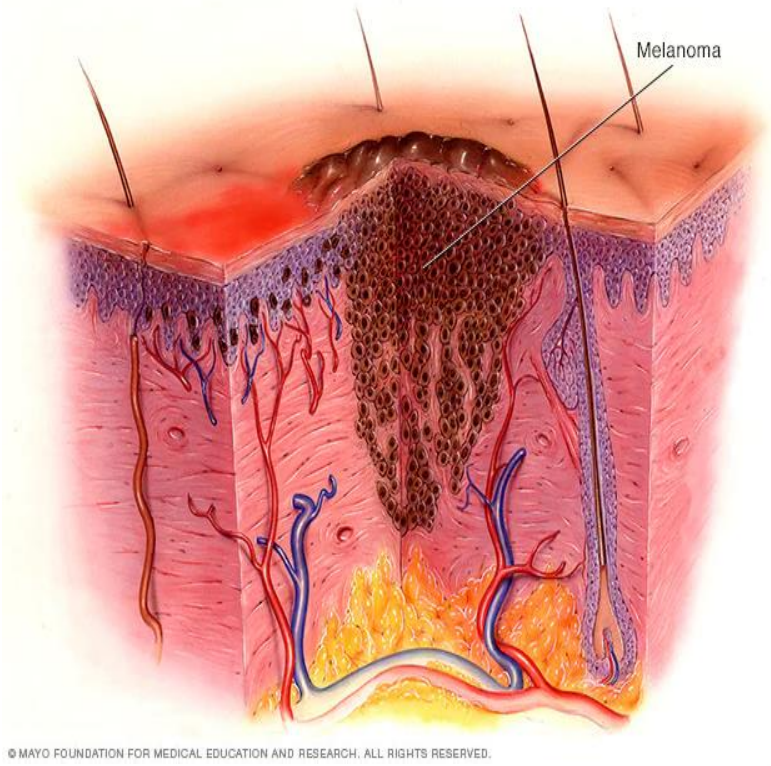
- Vitiligo
- Albinism
- Hyperpigmentation
- Pigment loss following skin damage

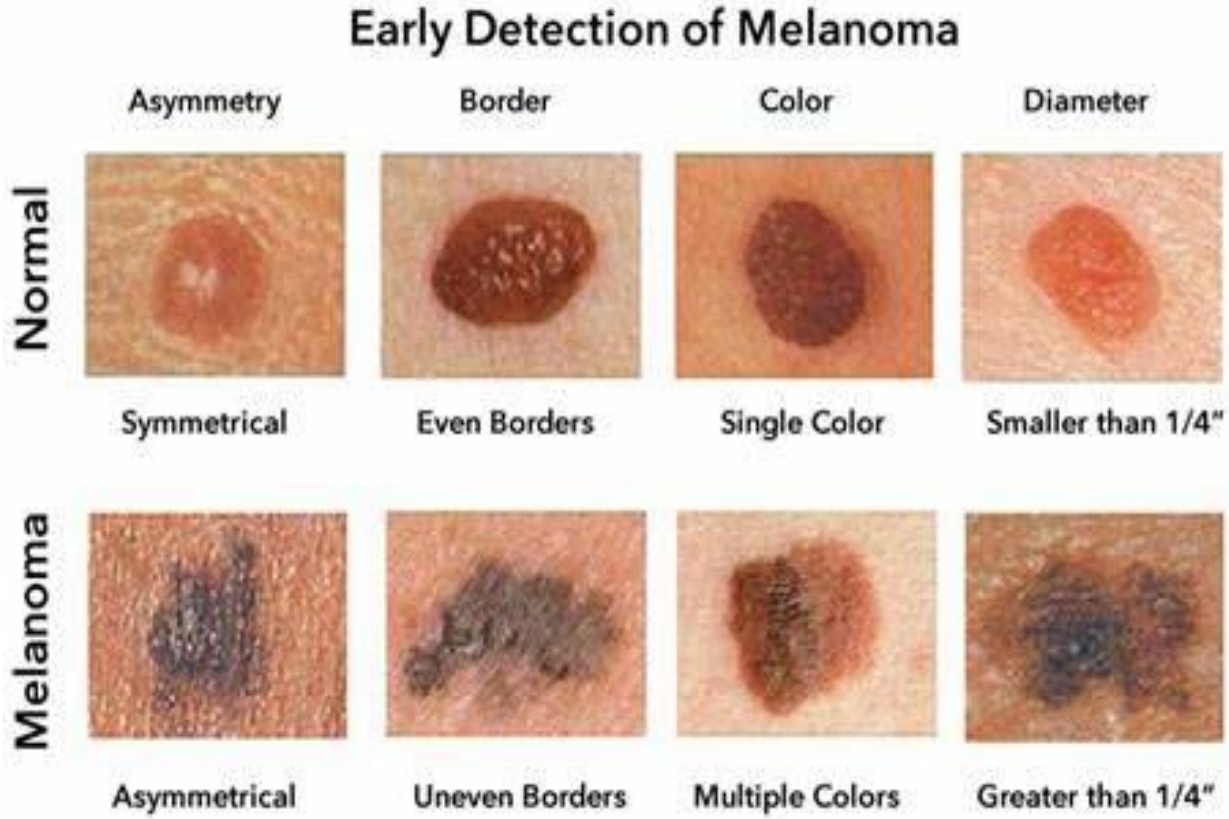
SUPERFADE, SOLUTIONS FOR UNWANTED PIGMENTATION

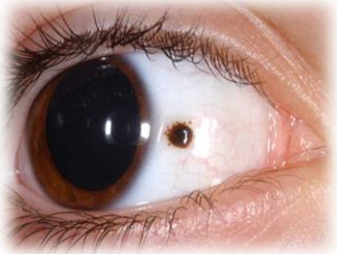
- Hearing loss
- Parkinson’s disease

Melanoma

- **Melanoma**, the most serious type of skin cancer, develops in the cells (melanocytes) that produce melanin the pigment that gives your skin its color. Melanoma can also form in your eyes and, rarely, inside your body, such as in your nose or throat.







Hyperpigmentation

- Hyperpigmentation is a common skin condition that occurs when certain areas of the skin become darker than the surrounding skin. This darkening is caused by an excess production of melanin.

Types of hyperpigmentation include:

Age spots, also called "liver" spots (Sunspots)

Melasma

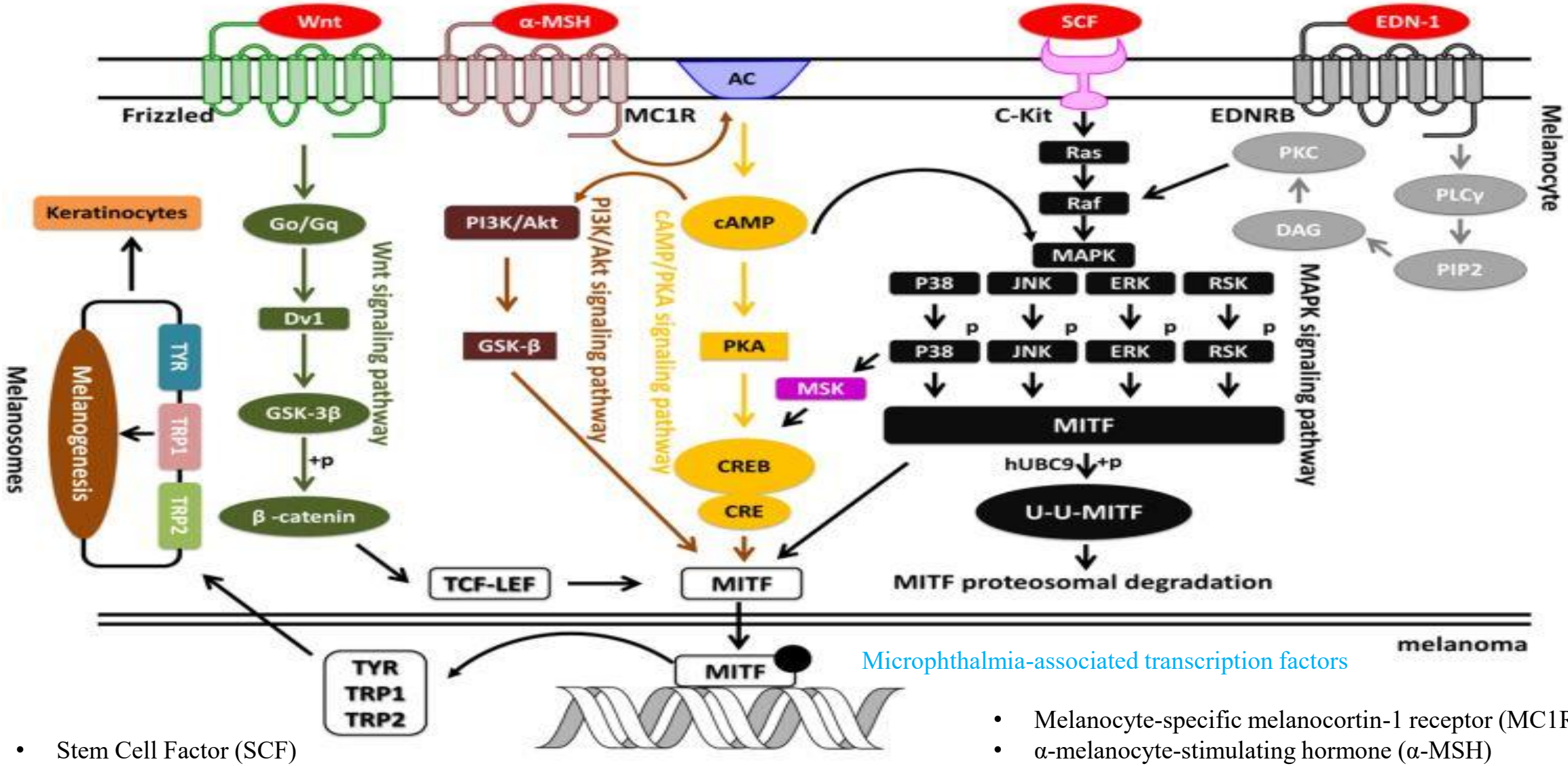
Post-inflammatory hyperpigmentation

Treatment:

Topical creams, chemical peels, laser therapy, microdermabrasion, and lightening agents.

Prevention is the best way to avoid hyperpigmentation.

Core regulatory pathways of melanogenesis

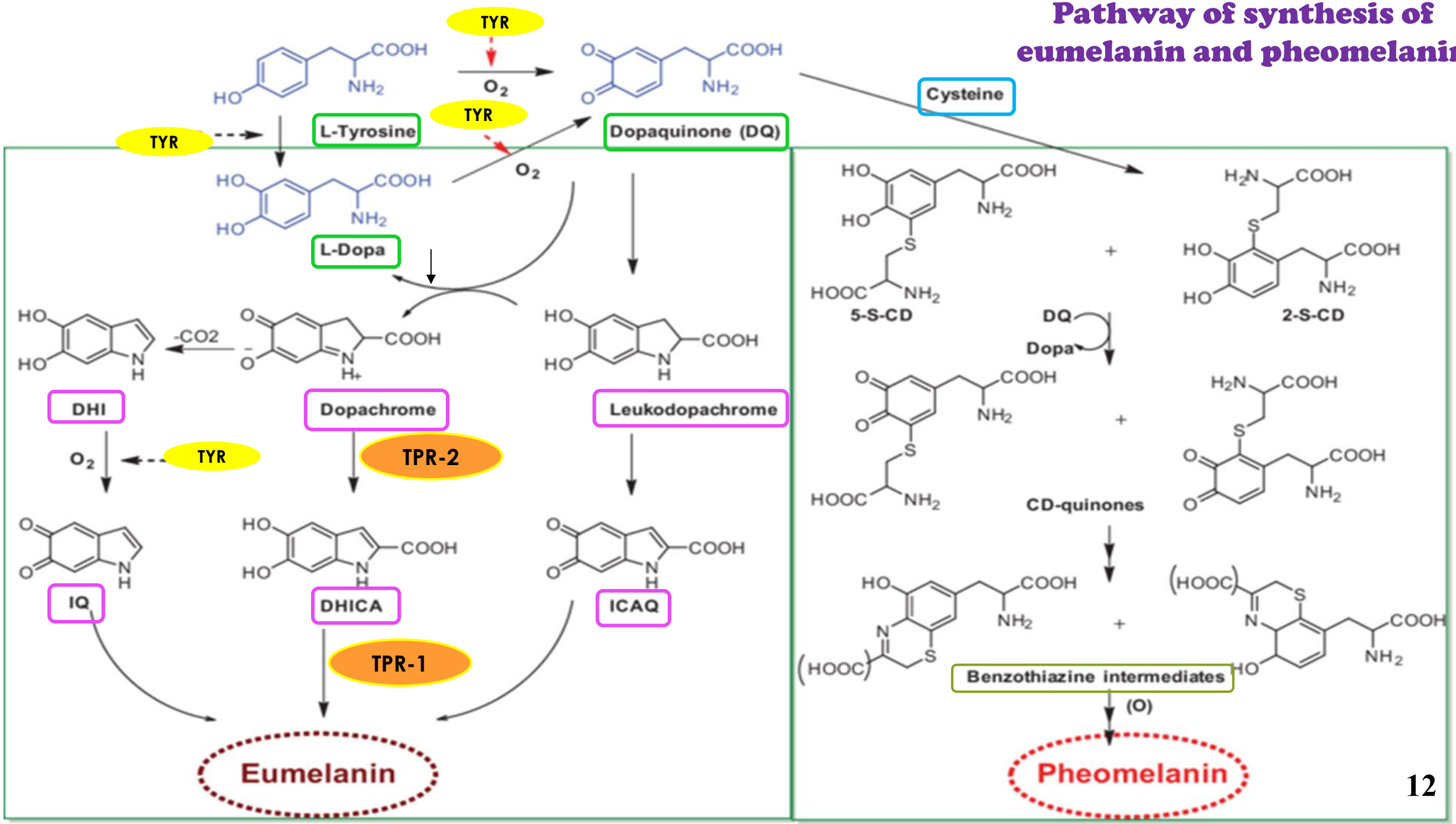


Microphthalmia-associated transcription factors

- Stem Cell Factor (SCF)
- Adrenocorticotropic hormone (ACTH)
- Agonist stimulating protein (ASP)

- Melanocyte-specific melanocortin-1 receptor (MC1R)
- α-melanocyte-stimulating hormone (α-MSH)
- Wingless-related integration site (WNT)
- MAPK/ERK Kinase (MEK)

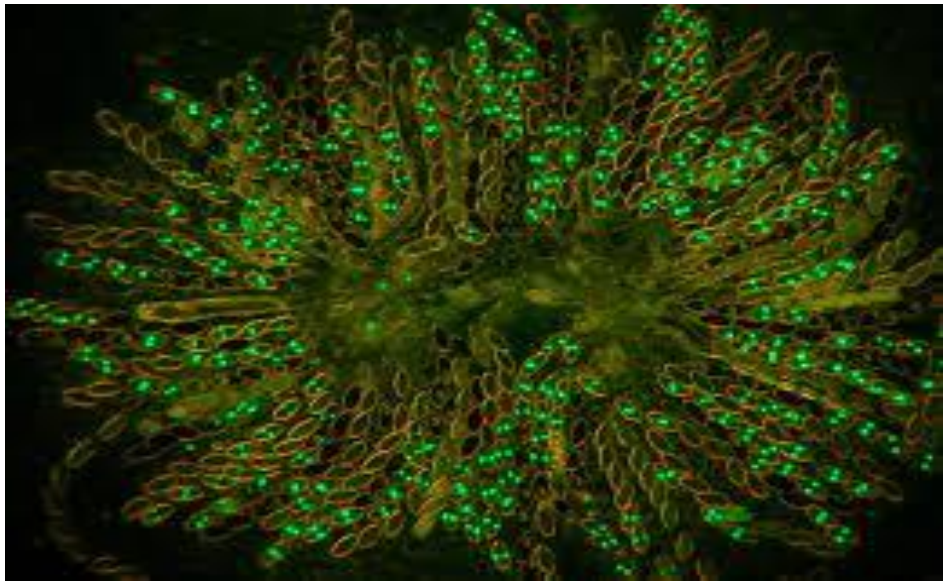
Pathway of synthesis of eumelanin and pheomelanin



Tyrosinase enzyme

- Tyrosinases have been isolated and studied from a wide variety of plant, animal, and fungal species. Tyrosinases from different species are diverse in terms of their structural properties, tissue distribution, and cellular location.

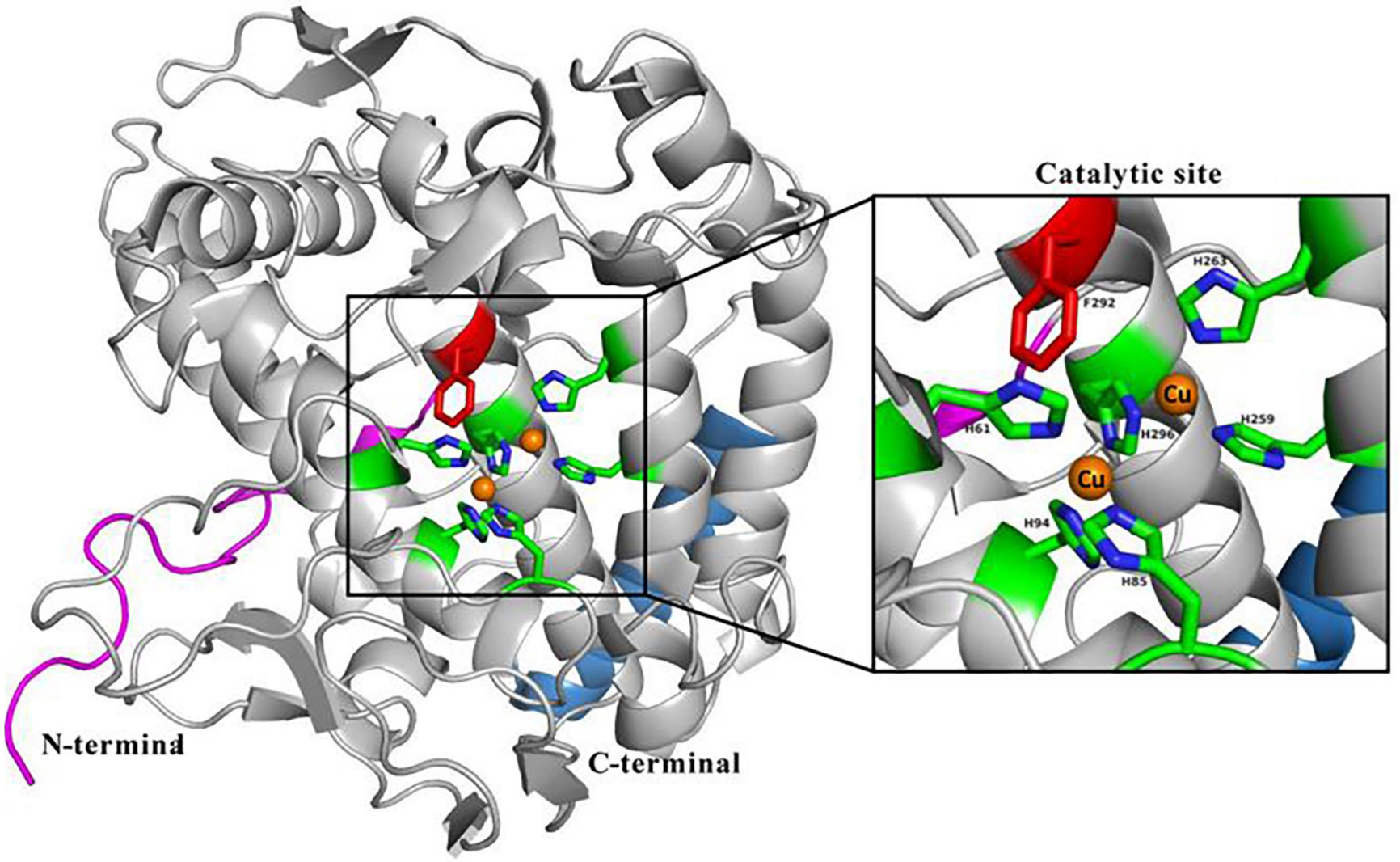
Agaricus bisporus



Neurospora crassa

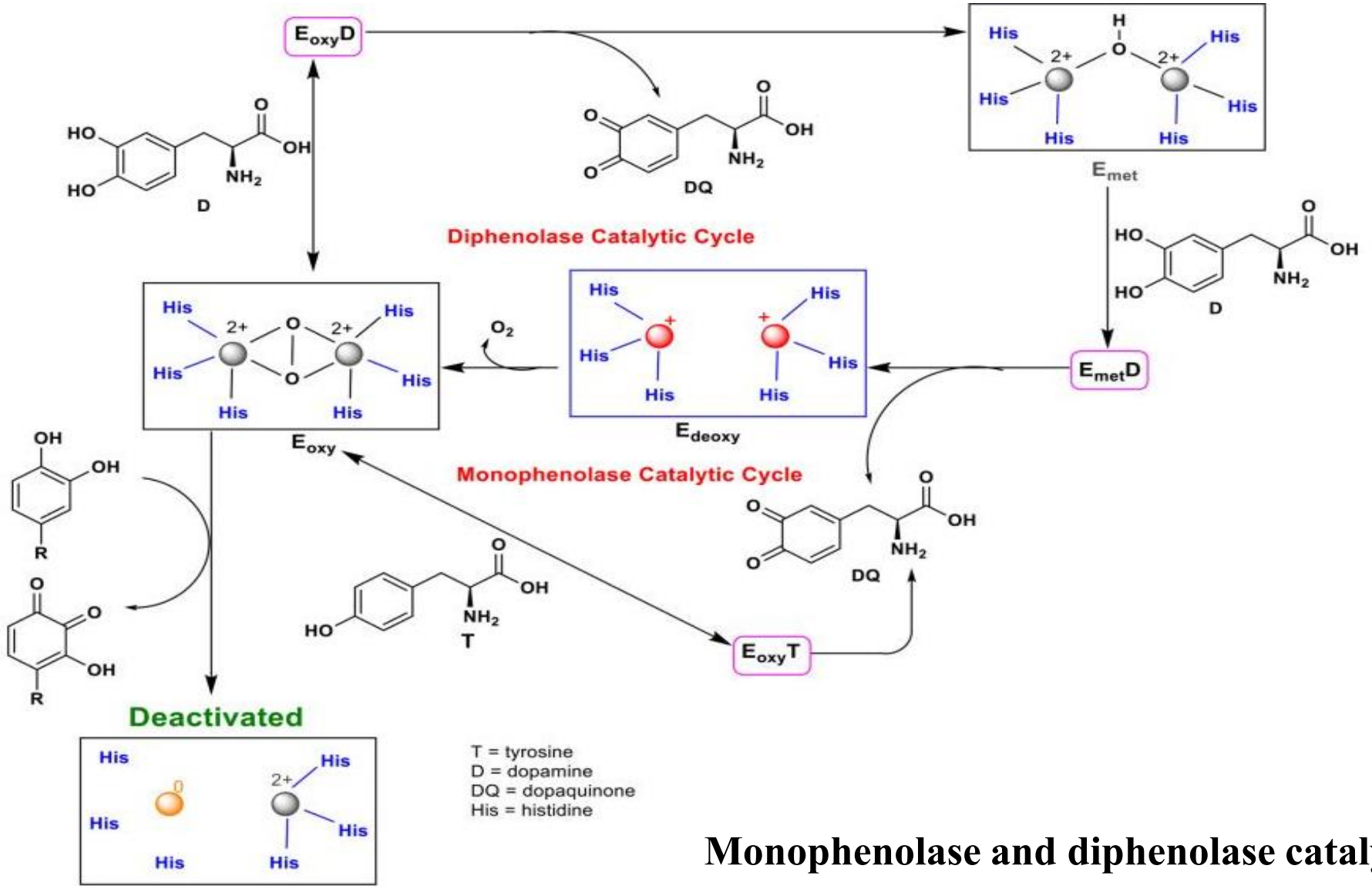
Tyrosinase enzyme

- Tyrosinase :
  - •Mono phenols
  - •Di phenols



The crystallographic structure of tyrosinase from Agaricus bisporus in deoxy form (PDB: 2Y9X)

Catalytic cycles of tyrosinase



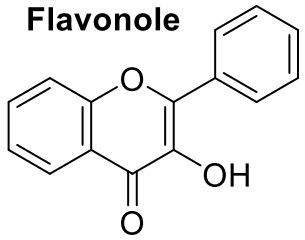
Monophenolase and diphenolase catalytic cycles

PART 2: TYROSINASE INHIBITORS

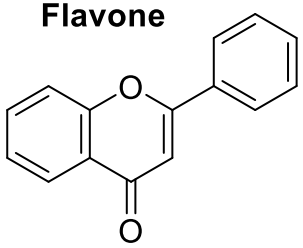
- **Natural and synthetic inhibitors of tyrosinase enzyme**

Flavonoids and derivatives

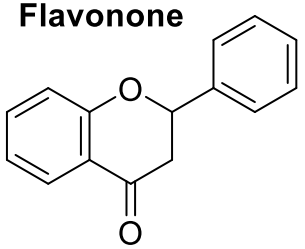
Flavonole

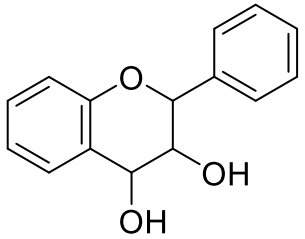


Flavone

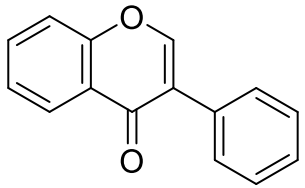


Flavonone

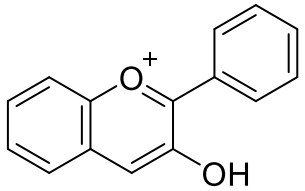




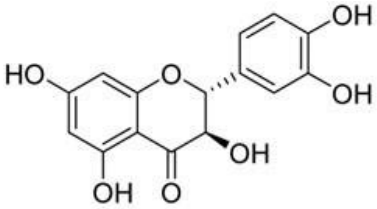
Flavandiol



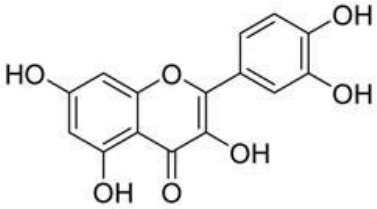
Isoflavone



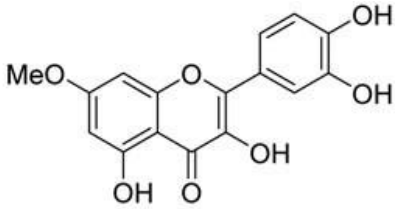
Antocyanidin



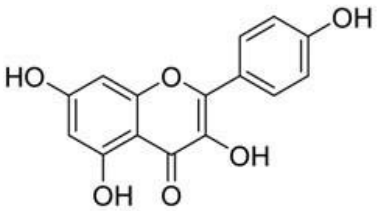
Catechin



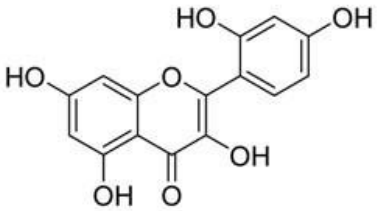
Quercetin



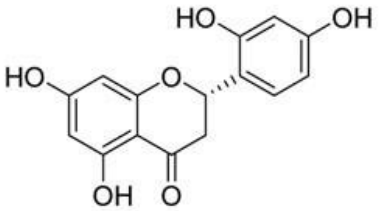
Rhamnetin



Kaempferol

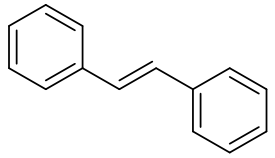


Morin

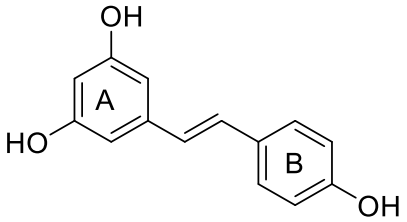


Steppogenin

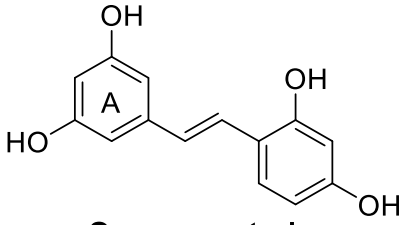
Stilbene and derivatives



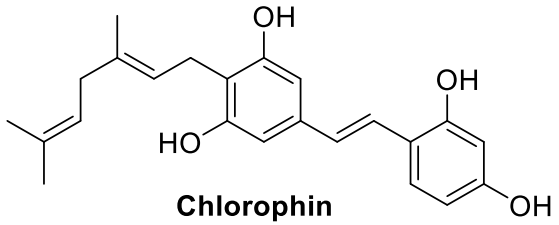
Stilbene



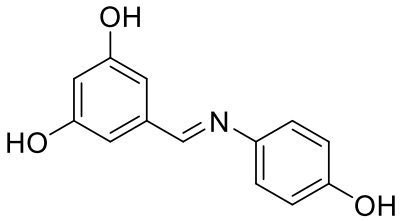
Resveratrol



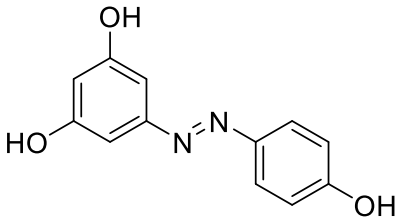
Oxyresveratrol



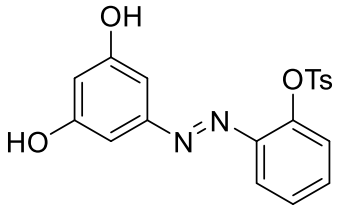
Chlorophin



(E)-4-((4-hydroxyphenylimino) methyl)benzene-1,2-diol

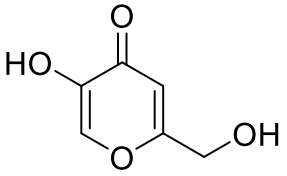


Azo-resveratrol

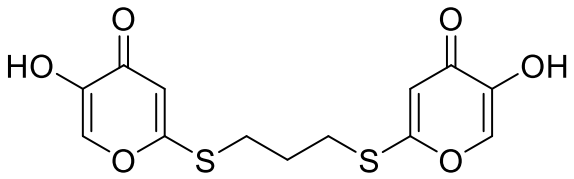


Toluene-4-sulfonic acid 2-(3,5-dihydroxy-phenylazo)-phenyl ester

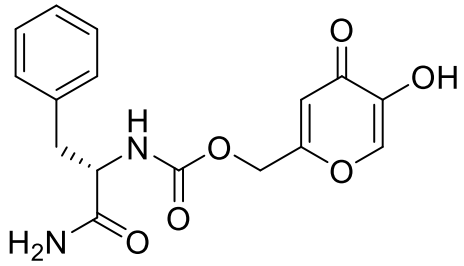
Kojic acid and derivatives



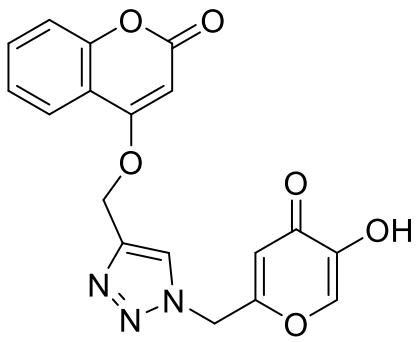
Kojic acid



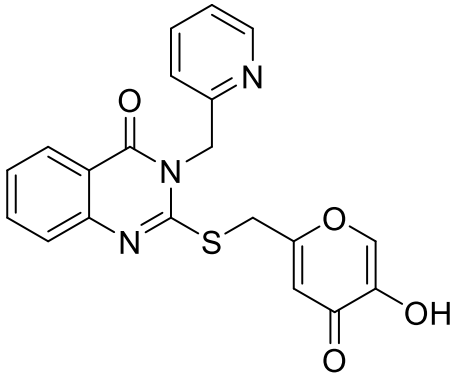
Dimer



Ka-F-NH2

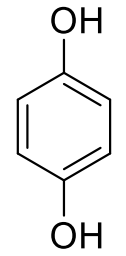


1,2,3-triazole- kojic acid (A)

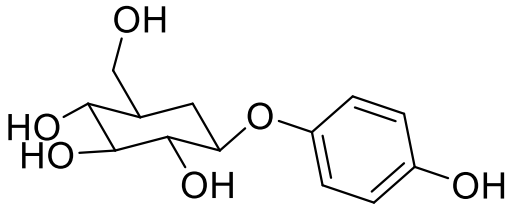


Quinazolinone-kojic acid (B)

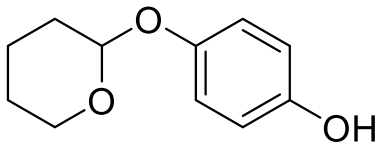
Hydroquinone and derivatives



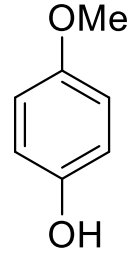
Hydroquinone



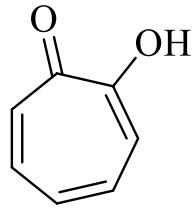
β-Arbutin



Deoxyarbutin

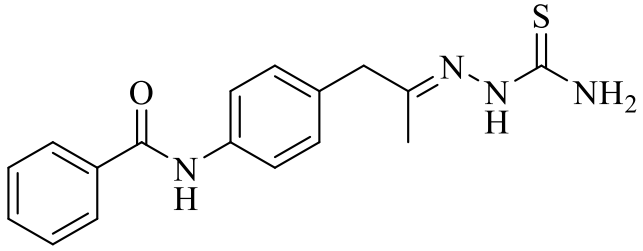


Mequinol



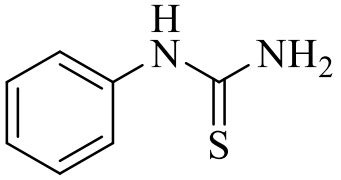
Tropolone

Thiosemicarbazone-type inhibitor

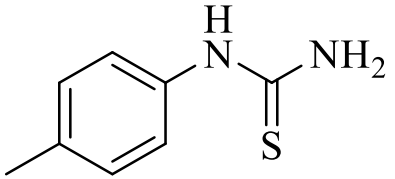


IC_{50} =0.291 μM, Kojic acid IC_{50} = 28.5 μM

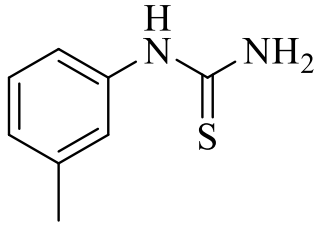
Thiourea derivatives



IC_{50} > 100 μM

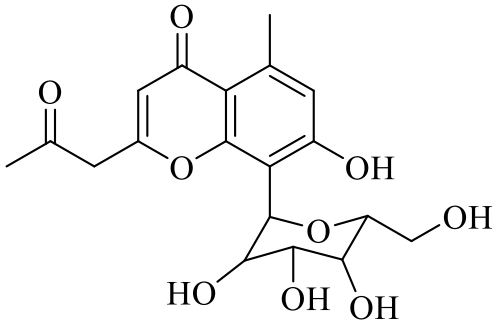


IC_{50} =1.4 μM

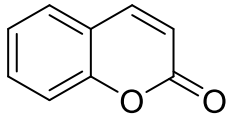


IC_{50} =0.6μM

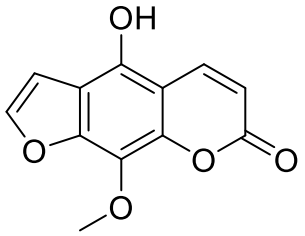
Aleosine



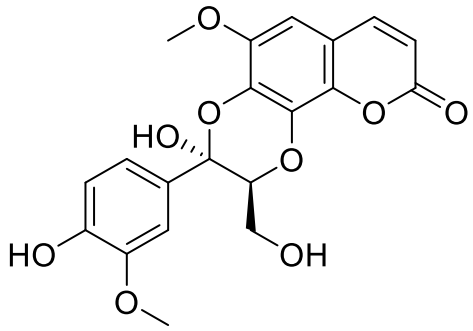
Chromene



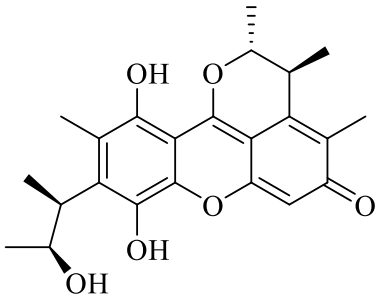
Coumarin



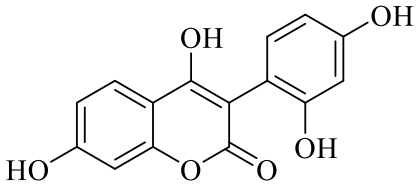
9-Hydroxy-4-methoxypsoralen



8´-epi-cleomiscosin A

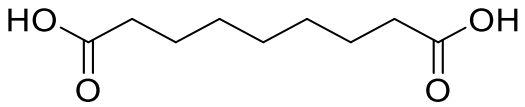


Pennicitrinone C

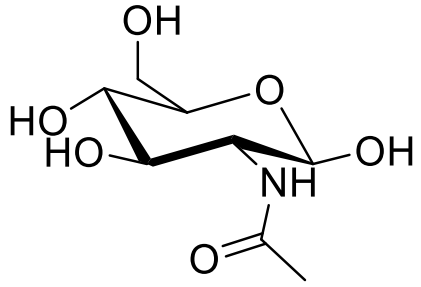


Asphodelin A

Coumarine



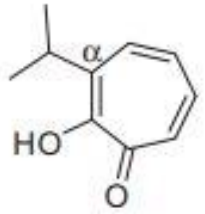
Azelaic acid



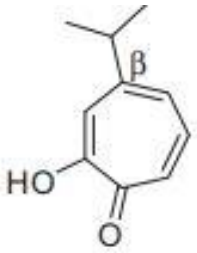
N-Acetylglucosamine

Human tyrosinase inhibitors

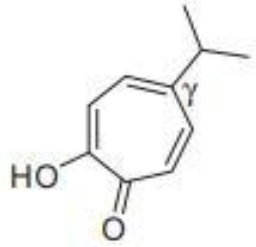
Thujaplicins (isopropyl cycloheptatrienolones) are a series of tropolone-related chemical substances that have been isolated from the softwoods of the trees of ***Cupressaceae*** family. These compounds are known for their antibacterial, antifungal, and antioxidant properties. They were the first natural tropolones to be made synthetically.



α-Thujaplicin (52)



β-Thujaplicin (53)



γ-Thujaplicin (54)

Compound	Tyrosinase inhibition IC50 (μM)	
	Human	Mushroom
α-Thujaplicin	>1000	9.53
β-Thujaplicin	8.98	0.09
γ-Thujaplicin	1.15	0.07
Kojic acid	571.17	53.70

- ✓ In thujaplicins, α,β- and γ were approximately 104.93-, 99.78-, and 16.43-fold, respectively, weaker inhibition against hTYR than mTYR.

The skin whitening agents include:

- Azelaic acid
- Cysteamine cream
- Vitamin C
- Niacinamide
- Kojic acid
- Retinoids (tretinoin)
- Hydroquinone (HQ)
- Arbutin (hydroquinone-β-D-glucopyranoside)
- Corticosteroids
- Glycolic acid peels
- Mequinol
- N-acetyl glucosamine
- N-acetyl-4-S-cysteaminylphenol
- Magnesium L ascorbyl-2-phosphate

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Thanks
for your attention