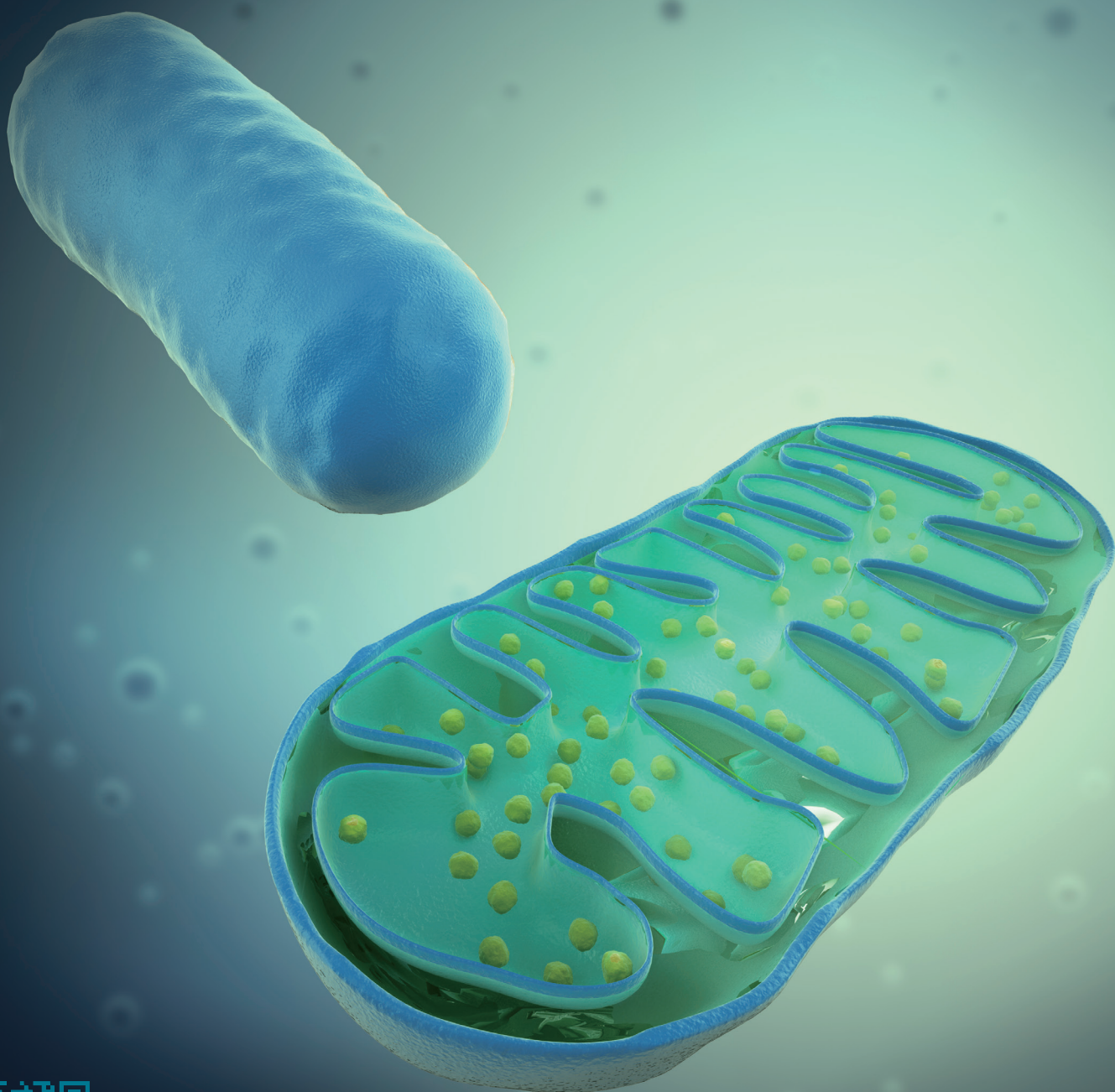


MitoCII Rejuvenate

Reverse the Age-Dependent Skin Aging



Find plant extract solution with

DermaLab

HOW TO FIGHT AGAINST MITOCHONDRIAL DYSFUNCTION

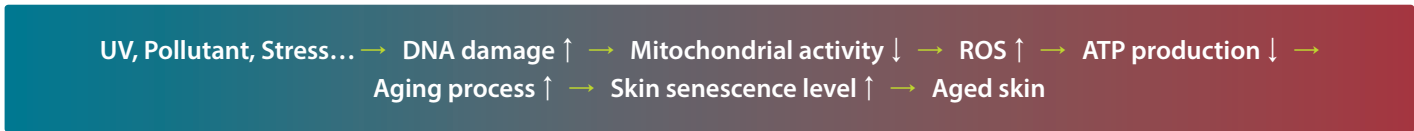
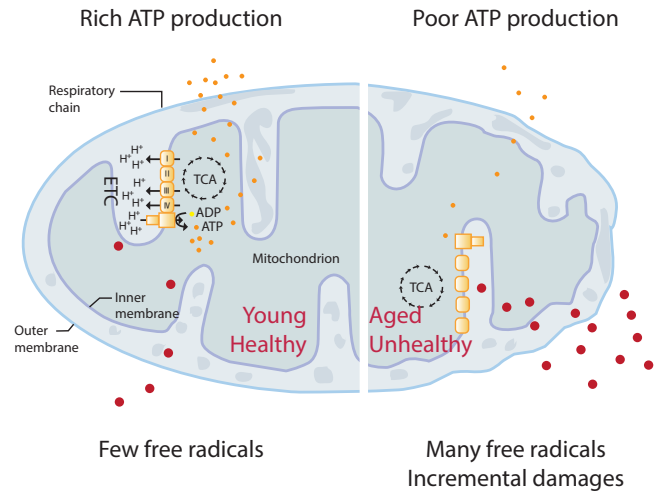
Mitochondria & Aging

Mitochondria, the powerhouse of a cell, produces energy by converting nutrients and oxygen into ATP through a Citric Acid Cycle (Krebs cycle, TCA cycle) and Electron Transport Chain (ETC). ATP is the chemical energy of the cell that powers the cell's metabolic activities.

The number of mitochondria in a cell depends on the metabolic requirements of that cell, and ranges from a single large mitochondrion to thousands. Humans need large amounts of energy in order to survive.

Mitochondria plays a key role in the aging process since skin aging mainly accompanies the mitochondrial dysfunction and ROS increase.

Maintaining healthy mitochondria is a crucial point to prevent dull and wrinkled skin texture.

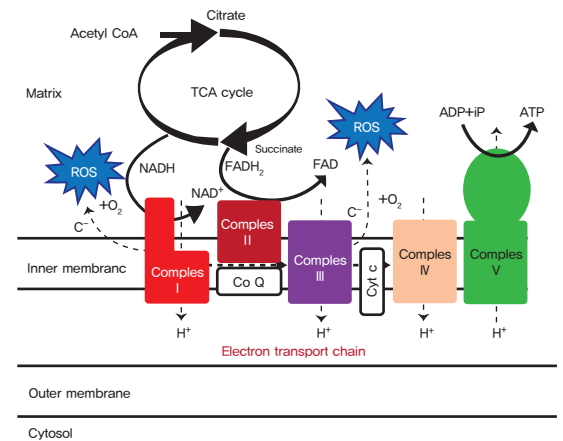


What makes the mitochondrial dysfunction?

Electron Transport Chain (ETC) is the final and most important step of ATP production. It consumes about 95% of the oxygen entering into the tissue cells.

ETC is composed of four multiprotein complex called Complex I-IV (V: ATP synthase). Direct link between TCA cycle and ETC is performed by Mitochondrial complex II which oxidizes succinate to fumarate and reduces ubiquinone. Complex II has a crucial role to connect the respiratory chain.

Unfortunately, ETC is a major generator of cellular oxidative stress which is an underlying cause of the aging process in skin. The impaired ETC not only works less efficiently in ATP synthesis but also generates more ROS.



• Reactive Oxygen Species (ROS)

ROS is produced by mitochondria as a byproduct of cellular respiration. It is an unstable molecule that contains oxygen and that easily reacts with other molecules in a cell. The accumulation of ROS in the cell may cause damage to DNA, RNA and proteins, and lead to a cellular dysfunction.

• Mitochondrial Complex Activity

IN FIBROBLAST : Complex II activity is age-dependently decreasing, Complex IV does not change.

IN KERATINOCYTE : No alteration in activity level of Complex II & IV with ages.

Fibroblasts are more sensitive to DNA damage, and also show much slower turnover rate. In addition to that, the level of complex II activity in fibroblast is much higher compared to the keratinocytes. Fibroblasts require more ATP to produce collagens, elastin, ECM and etc., and mitochondrial complex II plays a key role.

Young Skin => High level of Mitochondrial complex II activity & Abundant ATP & Less ROS
 Aged Skin => Low level of Mitochondrial complex II activity & Less ATP & Abundant ROS

MitoCII Rejuvenate

Gentiana Scabra is a widely distributed plant in Korea. According to the traditional Korean herbal medicine books, it has a bitter taste and cold energy which can relieve the heat energy in the human body.

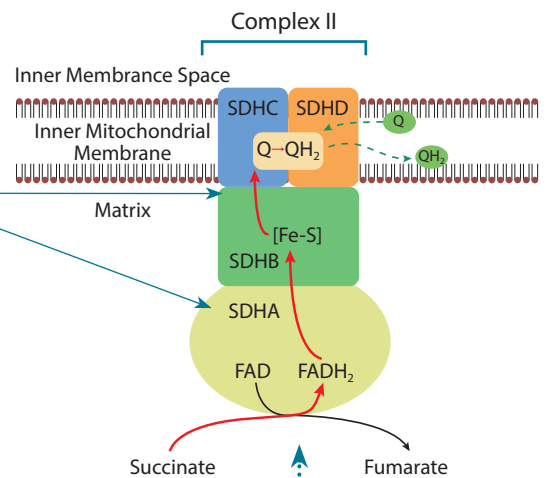
The root powder or the extract harvested and dried in shady place in autumn is used for various skin disorders since it has a good anti-inflammatory, anti-allergic and pain killing effect. It is also used for treating cancers in folk remedies. It is thought that the root has the potential to heal the dysfunctional-cells.



MECHANISM

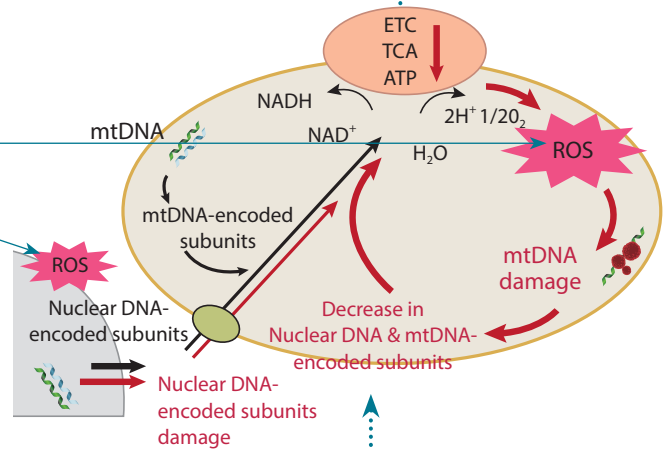
Increase the expression of subunits of Mitochondrial Complex II

The transcript expression levels of the complex II subunits SDHA and SDHB decreases with age in fibroblasts. Stimulating the expression results in reversing the ATP production to young and healthy stage.



Reduce ROS to protect DNA damages

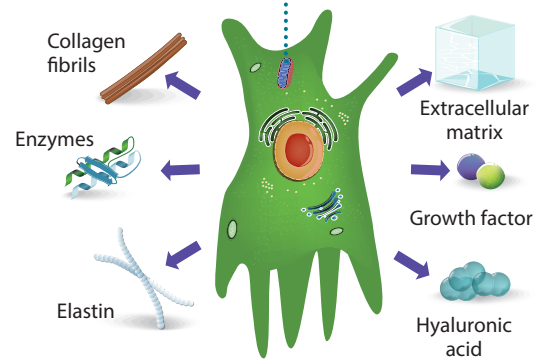
ROS generation and accumulation in skin cause damages to cellular components and a decrease of tissue function.



Reverse fibroblasts to young and healthy condition

Fibroblasts can produce more collagen, elastin, ECM and etc. with an abundant ATP and low level of oxidative stress.

Elastic and wrinkleless skin texture can be achieved through this age-reversing process.



IN-VITRO TEST

MITOCHONDRIAL COMPLEX II SUBUNIT EXPRESSION EFFECT

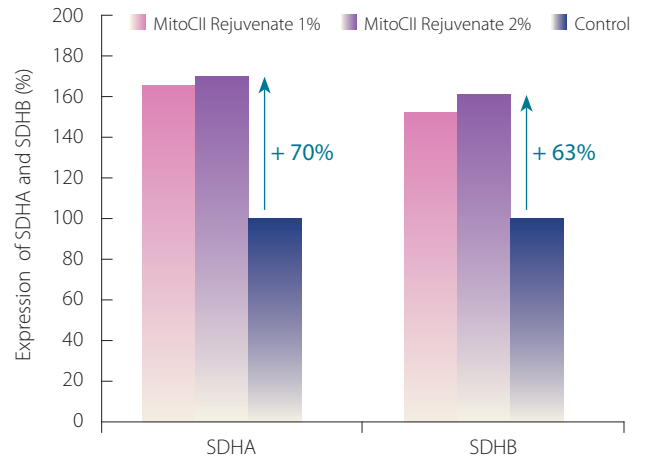
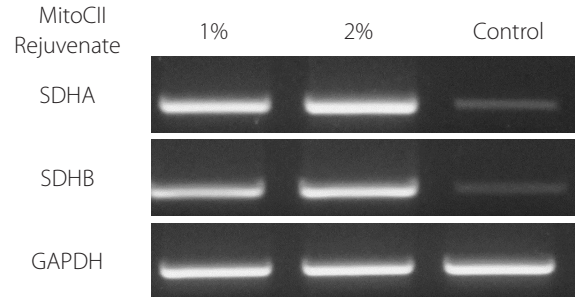
Flavoprotein subunit of succinate dehydrogenase (SDHA) and Iron-sulfur protein subunit of succinate dehydrogenase (SDHB) are involved in complex II.

They are responsible for transferring electrons from succinate to ubiquinone (coenzyme Q) in the mitochondrial electron transport chain.

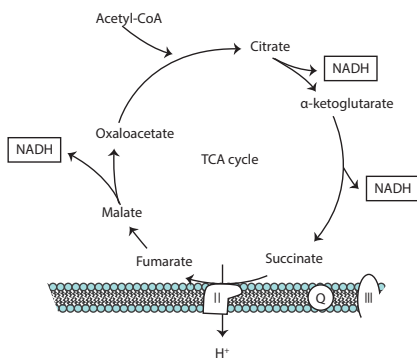
The activity of these subunits in fibroblast decreases with age. Defects in SDHA and SDHB are a cause of mitochondrial complex II deficiency.

The expression of SDHA : 70% ↑
The expression of SDHB : 63% ↑

Protocol: Human dermal fibroblast (HDFa) cultures were incubated during 36 hours (at 37°C, CO₂: 5 %) in presence of MitoCII Rejuvenate. The expression levels of mRNA were analyzed by RT-PCR.



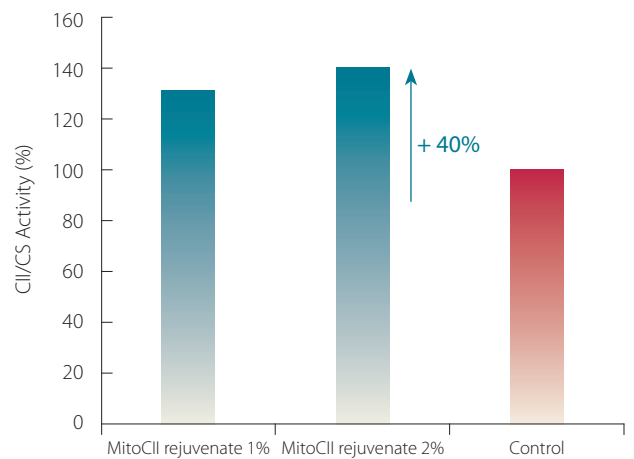
MITOCHONDRIAL COMPLEX II ACTIVATION EFFECT



Mitochondrial complex II is one of the five complexes involved in oxidative phosphorylation in the inner mitochondrial membrane and also a member of the tricarboxylic acid cycle (TCA).

Citrate synthase is the initial enzyme of the tricarboxylic acid (TCA) cycle. Mitochondria citrate synthase activity is measured by the amount of mitochondrial complex II in reaction.

CII/CS Activity : 40% ↑



Protocol: Human dermal fibroblast (HDFa) cultures were incubated during 36 hours (at 37°C, CO₂: 5 %) in presence of MitoCII Rejuvenate. Complex II activity was measured by citrate synthase activity (CII/CS).

IN-VITRO TEST

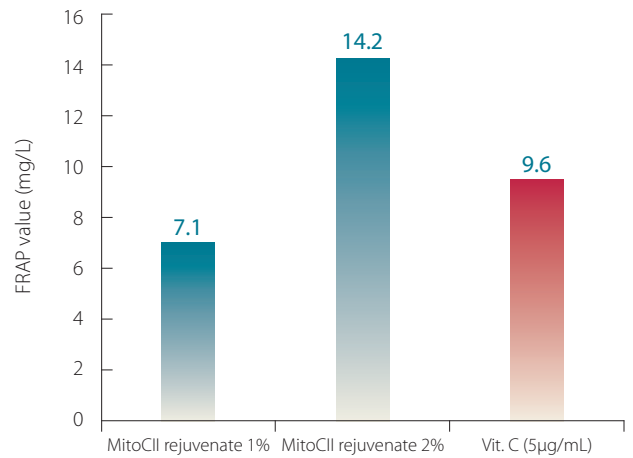
ANTIOXIDANT EFFECT

Mitochondrial free radicals, produced during normal metabolism and various skin disorders, cause oxidative damage.

Mitochondrial dysfunction is associated with ROS, and this accelerates ROS production. The excessive ROS accumulation will lead to cellular aging such as damage to DNA, proteins and lipid membranes.

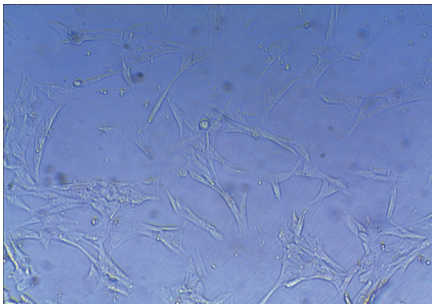
Ferric Reducing Antioxidant Power (FRAP) Assay is a quantitative assay for measuring the antioxidant potential.

Protocol: OxiSelect™ Ferric Reducing Antioxidant Power (FRAP) Assay Kit (CELL BIOLABS, INC.). Vit. C : Vitamin C (Positive Control)

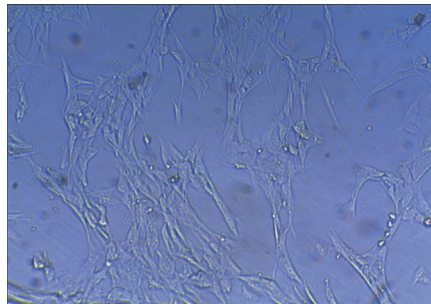


FIBROBLAST PROLIFERATION EFFECT

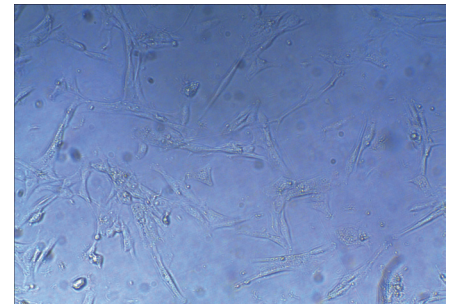
MITOCII REJUVENATE ENHANCES THE PROLIFERATION OF FIBROBLAST at 2%



MitoCII Rejuvenate 1%



MitoCII Rejuvenate 2%



Control

Protocol: Human dermal fibroblast (HDFa) cultures were incubated during 36 hours (at 37°C, CO₂: 5 %) in presence of MitoCII Rejuvenate. Images were captured by the Optivision Image Capture system.

IN-VIVO TEST

WRINKLE REDUCTION EFFECT

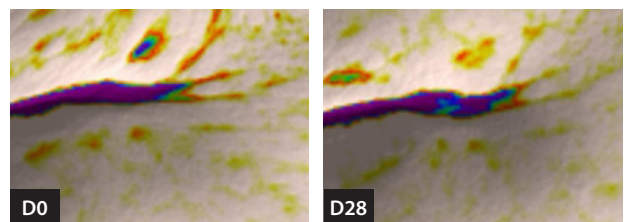
MITOCII REJUVENATE DECREASES THE CROW'S FEET

2% MITOCII REJUVENATE cream reduces the Crow's feet intensity

-19.6 % on average after 28 days and up to -21.8 %

Method : Measurement of Crow's feet.

Application of 2 % MITOCII REJUVENATE Cream for 4 weeks and measurements. Crow's feet was evaluated by Antera 3D (Miravex Limited).





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Cosmetic activities	<ul style="list-style-type: none">• Increase Mitochondrial Complex II subunit expression• Increase Mitochondrial Complex II activity• Antioxidant effect• Cell Proliferation effect
INCI name	<ul style="list-style-type: none">• MitoCII Rejuvenate Water (and) Butylene Glycol (and) Phenoxyethanol (and) Ethylhexylglycerin (and) Gentiana Scabra Root Extract• MitoCII Rejuvenate (HD) Water (and) Butylene Glycol (and) 1,2-Hexanediol (and) Gentiana Scabra Root Extract
Recommended % of use	MitoCII Rejuvenate 2% MitoCII Rejuvenate (HD) 2%