The Active Ingredients Mixture of Olives Provides Skin Whitening and Age Spot Reduction

Author: Maria Lueder, Qenax AG, Switzerland

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Abstract
The olive tree, *Olea europaea*, is native to the Mediterranean basin and parts of Asia Minor. Native olive oil has often been used in cosmetic formulations but other interesting ingredients from the fruit and the leaves for a long time were not investigated for use in cosmetic products. The fruit and the leaves contain high amounts of polyphenols. The major polyphenol is Oleuropein. With increasing maturity of the olive hydroxytyrosol will be released from the Oleuropein, which is even stronger in anti-oxidative power than the Oleuropein.

A standardised olive extract (Tradename: Cayoma® Olive) containing high amounts of polyphenols and hydroxytyrosol has been prepared to evaluate skin whitening and age spot reduction effects. The cosmetic active was tested both *in vitro* and *in vivo*.

Melanin reduction as a direct measure for skin lightening properties and age-spot reduction was measured *in vitro* on primary human melanocytes. Additionally glutathione was also measured *in vitro* on primary human melanocytes. A high glutathione level in melanocytes directs the production of melanin into the soluble and lighter brown pheomelanin versus dark and insoluble eumelanin which supports skin lightening.

The *in vivo* test was designed as a double blind, placebo controlled study on the hands of twelve Caucasian female volunteers aged between 46 and 72. The study duration was three months, with readings before the first application, after four, eight and twelve weeks.

A significant melanin reduction of up to 50% and a significant increase of the glutathione level up to 55% could be measured *in vitro*. The confirmation *in vivo* showed not only a significant reduction of age spot colour but also a colour reduction of the whole skin area on the hands.

Introduction
Hippocrates used olive leaves for wound healing and Dioskurides applied them in fomentations against skin inflammation, abscess thrush and slowly healing wounds. Today it is known that the high polyphenol content with powerful anti-oxidative properties is responsible for these effects.

Depending on the olive’s degree of ripeness, these secondary plant components are found in the cold pressed oil (approx. 0.1%) and develop effects similar to omega-3 fatty acids, especially the Oleuropein. With increasing maturity of the olive, hydroxytyrosol will be released which is stronger in anti-oxidative power (Figure 1). Like resveratrol, hydroxytyrosol is a very strong antioxidant. As hydroxytyrosol is amphiphilic, it can develop its effect as a powerful radical scavenger in lipophilic cell membranes as well as in the hydrophilic cell plasma.

Publications show that hydroxytyrosol protects human melanocytes *in vitro* from protein damage, induced by long-wave UV light, and reduces the release of inflammation inhibitors like Cox-2 in macrophages.

Glutathione is a peptide, consisting of three amino acids: Glutamic acid, Cysteine and Glycine. It is present in almost all cells in higher concentrations and belongs to the most important natural antioxidants of the body. At the same time it is a reservoir for Cysteine. Glutathione protects cellular macromolecules like proteins and membrane lipids against free radicals (reactive oxygen species ROS). An increased level of glutathione stimulates the formation of the lighter and soluble pheomelanin versus the darker, insoluble eumelanin. Tyrosinase, the rate limiting enzyme of melanogenesis, catalyses the hydroxylation of L-tyrosine to DOPA and the oxidation of DOPA to DOPAquinone. If cysteine or glutathione is present, it reacts with DOPAquinone to produce cysteinylDOPA and the benzothiazine derivatives of pheomelanin (Figure 2).

Cayoma® Olive, a standardised extract from olive fruit and olive leaves with a high content of active ingredients has been developed and tested against age spots and for skin lightening *in vitro* and *in vivo*.