

A patented* olive fruit extract for a healthy skin

.....
Double standardization
in polyphenols and
verbascoside

.....
Clinical and
pharmacological data
support its efficacy

.....
Specifically designed
for topical and oral
formulations

.....
A safe product, devoid of
any side effect



Opextan™

■ **Symbol of the Mediterranean culture**, the olive tree has gained interest for its superb properties of various kind. The tree, in fact, is extremely long living, and this is also due to its content of **potent antioxidant compounds**.

Since the most ancient times, both Pliny and Hippocrates used to prescribe **medications from olive** as a cure for a number of disorders, from inflammation to nausea. Many of these old remedies have passed into folk medicine and are still as relevant today as they were hundreds of years ago.

Recently, the beneficial health properties of olive oil and fruit consumption have been correlated to a decreased incidence of various diseases in the Mediterranean area, as long-term consumption of a Mediterranean-type diet is associated with a lower incidence of cardiovascular and other free-radical mediated diseases,¹ and also to a **less abundant formation of skin wrinkles**.

Epidemiological studies, in fact, have shown a negative correlation between the consumption of olive fruits and olive oil containing a good deal of antioxidant substances (**polyphenols**) and wrinkle formation. This research indicates people who consume a high intake of olive fruits and oil have fewer wrinkles.²

Olive polyphenols exert a free radical scavenging activity that has a direct impact on skin health, as they **prevent oxidative damage** related to wrinkle formation, skin thinning, dehydration, etc.. The scavenging and antiinflammatory ability of olive polyphenols appear to be one of the treatments of choice for skin care in terms of **wrinkles and aging prevention**.

A natural clinically-proven aid for a healthy and beautiful skin

Opextan™ is a standardized olive fruit extract obtained by a selected variety of olive possessing a unique polyphenolic profile: it contains **verbascoside**, a polyphenol characteristic of the olive fruit which is not present in the leaves. Verbascoside, due to its potent biological effects as a radical scavenger, has been selected as the **reference compound** of the extract standardization.

- **≥10%** total polyphenols
- **≥ 2%** verbascoside

Its protecting activity is supported by **three clinical trials**, both for **oral and topical application**, and by extensive pharmacological data.

Clinical studies

The efficacy of Opextan™ was verified both by oral and topical application, targeting in particular skin care and skin health. With this aim, Opextan™ has been administered orally or topically to groups of subjects in order to evaluate the antioxidant capacity of the product and its beneficial effects on skin health. It was proven **effective in improving antioxidant defences and in counteracting the oxidative stress**.

■ decrease of skin sensitivity to UV irradiation^{3,4}

Opextan™ was administered orally at a dose of 160 mg/day for 4 weeks to 13 male subjects in a placebo controlled trial. The subjects were irradiated by ultra violet light (UVA + UVB 0.45 mW/cm²) from 0.054 to 0.135 J/cm² successively on the dorsal area. The minimum erythmal dose (MED) was measured before and after Opextan™ treatment. Opextan™ promoted a mean increase of the MED by 16.45%, suggesting a lower sensitivity of the volunteers' skin to UV irradiation (fig. 1).

*Antioxidant defenses,
also by oral route, protect
skin damages induced by
UV irradiation*

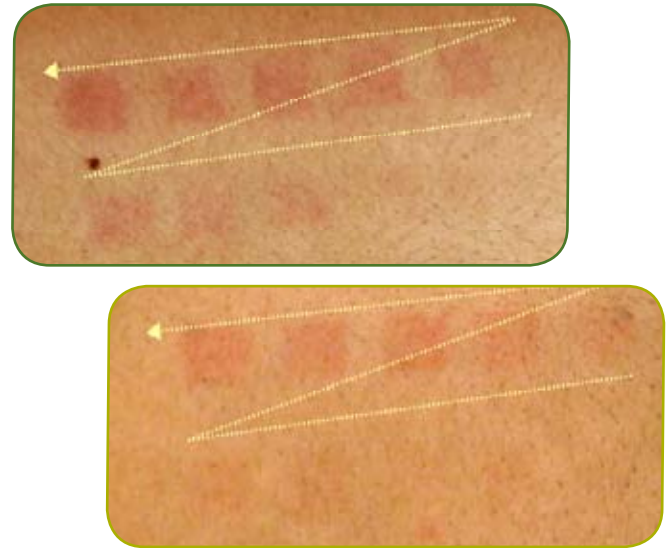


Fig. 1: effect of Opextan™ on skin sensitivity to UV irradiation, image taken before and after the treatment

■ improvement of oxidative status in healthy volunteers^{3,4}

Oxidative stress appears to be the cause of the onset of several degenerative disorders; epidemiological studies suggest that a high intake of dietary antioxidants is protective.

To evaluate the antioxidant effect of Opextan™ in volunteers, the *in vivo* peroxidation was evaluated by the quantification of the oxidative marker 8-isoprostane (8-iso-prostaglandin F_{2α}).⁵

Nineteen healthy volunteers received Opextan™ at a daily dosage of 400 mg for 4 weeks. The urinary excretion of 8-isoprostane was evaluated in urine samples before the beginning of the study and at the end of the 4 weeks' treatment. Opextan™ significantly decreased the formation of the oxidative marker (47%, mean data, chart 1).

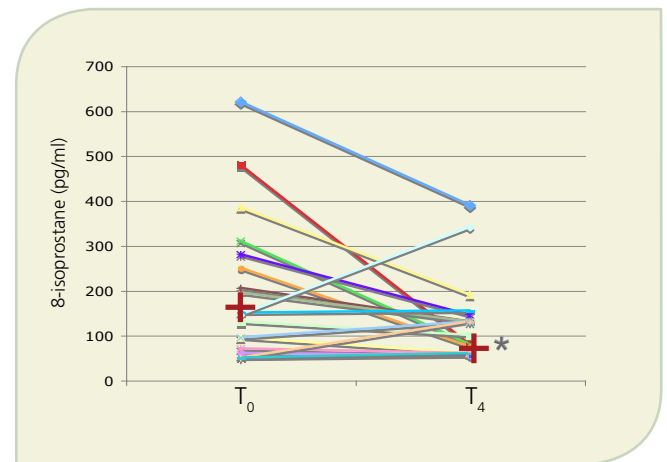
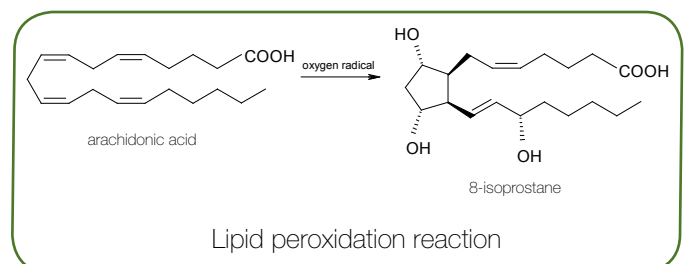


Chart 1: effect of oral administration of Opextan™ on lipid peroxidation



■ reduction of lipid peroxidation by topical application⁴

Lipid peroxidation is a well known example of oxidative damage in lipid containing structures.⁶ Lipid hydroperoxides are prominent non-radical intermediates for lipid peroxidation.

The effect of topically applied Opextan™ was evaluated on a group of 6 healthy volunteers who were asked to wash their face and apply the Opextan™ containing formulation at 0.5% and the placebo formulation on each half face. After three hours they were irradiated with sunlight for about 20 minutes. Sebum was sampled, extracted and measured by dosing luminescence in 0.1 µg/ml recovered sebum. Luminescence indicating lipid peroxidation in the Opextan™ treated area, decreased by 27.1% (chart 2).

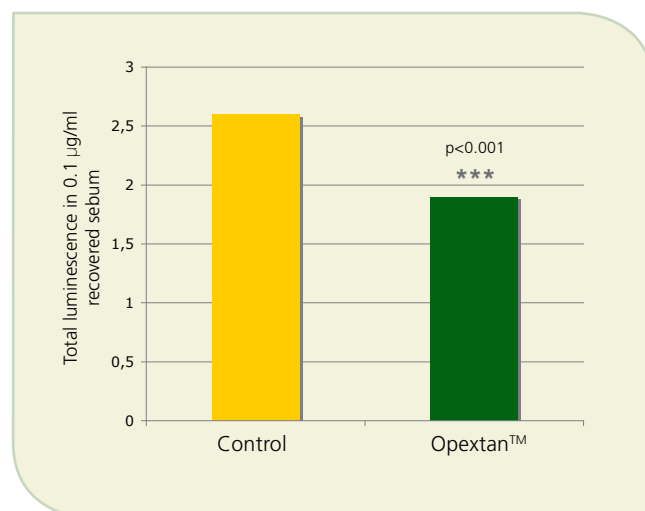


Chart 2: effect of Opextan™ on lipid peroxidation by topical application

Pharmacology

Opextan™ protects from lipid peroxidation both by oral and topical application

The pharmacological profile of Opextan™ has been defined by *in vitro* and *in vivo* experimental studies. For the *in vivo* studies verbascoside, a polyphenol concentrated from the extract, was utilized.

■ *in vitro*⁶⁻⁸

• antioxidant activity

Opextan™ antioxidant activity was evaluated by using the stable free radical DPPH (1,1 diphenyl-2-picrylhydrazyl). Opextan™ exerted an interesting reducing effect on DPPH, with an IC_{50} of 0.0054% after 20 minutes.

Furthermore, the radical scavenging ability of single polyphenols present in the extract (verbascoside, hydroxytyrosol and caffeic acid) was compared to two reference compounds as ascorbic acid and oleuropein (the most characteristic polyphenol present in the olive leaves). Verbascoside turned out to be five times more active compared to oleuropein (chart 3).

Additionally, Opextan™ polyphenols were tested for their scavenging activity on superoxide anion $O_2^{\cdot-}$. This model mimics more closely the *in vivo* situation, as the formation of the superoxide anion is physiological: the harmful effects of UV exposure on the skin, for instance, are associated with the formation of reactive oxygen species, such as superoxide radical.⁹ Verbascoside was tested at 0.016 mM concentration, and inhibited superoxide anion formation by 68%.

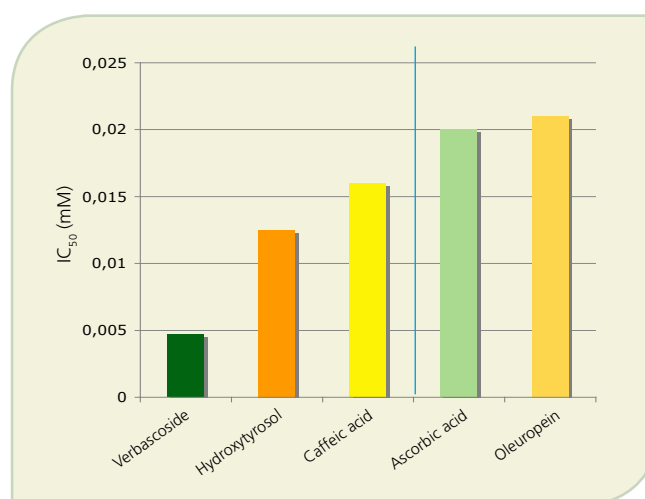


Chart 3: DPPH scavenging activity of Opextan™ polyphenols

Opextan™ inhibits superoxide anion formation

● **glucose management activity**

The number of diabetic patients increases rapidly, and the pathology, including potential patients, is affecting one in six adults. One of the symptoms of diabetes is water metabolic disorder,¹⁰ but also in healthy people there is evidence that high blood glucose level is related to skin moisture loss. Blood glucose levels are important in affecting skin care, too. Opextan™ was tested in the α -glucosidase activity template test and exerted a good inhibition of the enzymatic activity, thus suggesting a synergy with the free radical scavenging activity (chart 4).

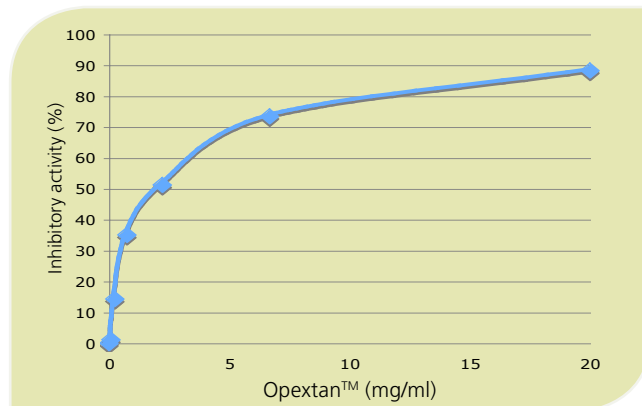


Chart 4: effect of Opextan™ on α -glucosidase activity

■ **in vivo**

● **protection from epidermal permeability barrier¹¹**

UV irradiation induces several cutaneous responses among which disruption of epidermal permeability barrier, measurable by TEWL (Trans Epidermal Water Loss) modification.

Adult hairless mice (4-5 animals per group) were exposed to a single dose of UVB on day 7 of oral treatment with verbascoside. Mice were administered dosages of verbascoside from 125 to 6.25 mg/kg via oral gavage daily for 11 days. TEWL was measured on day 0, day 3 and 4 after UV exposure. TEWL decreased significantly (chart 5), thus indicating a protective action exerted by verbascoside.

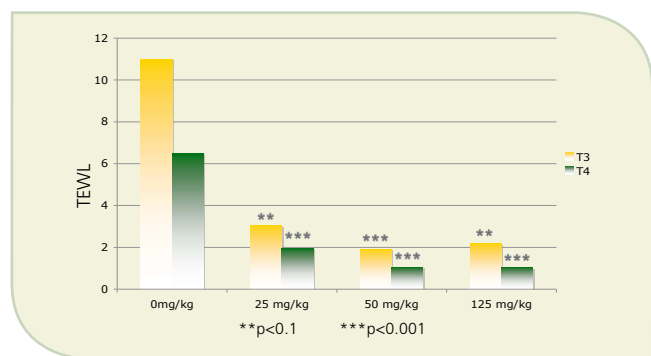


Chart 5: effect of verbascoside on UV induced epidermal permeability barrier damages

● **prevention of wrinkle formation**

Photoaging and wrinkle formation may be promoted by UV irradiation.

Adult hairless mice (8 animals per group) were exposed to increasing doses of UVA and UVB (starting from 20J UVA and 20J UVB per cm² to reach the doses of 30J and 40J per cm² respectively from week 3 to 12). Irradiation was performed 5 times per week for 12 weeks, with verbascoside dosing beginning on week 5 at 6.25 or 25 mg/kg/day. Wrinkle formation in each animal was determined according to the grading scale as indicated in table 1:

Grading value	Signs observed
0	no wrinkling or laxity; fine striations running the length of the body
1	disappearance of all fine striations
2	a few deep wrinkles and laxity
3	increased deep wrinkles

Table 1: grading scale of wrinkle formation observation

Verbascoide, Opextan™ most characteristic poly-phenol, promoted a prevention of UV induced wrinkle formation by 38% (25 mg/kg dose, p<0.001).

These data have been additionally confirmed by the objective measure of epidermal thickness,¹² which is a useful parameter to evaluate cutaneous inflammation induced by UV.

Epidermal thickness was reduced by 28%.

Opextan™ prevents UV induced photoaging and wrinkle formation



Conclusive remarks

The antioxidant and radical scavenging capacity of **Opextan™** has demonstrated its **beneficial effects at skin level**, where free radical mediated degeneration such as wrinkle formation, epidermal barrier disruption, etc., may be effectively prevented. The effectiveness of the product has been demonstrated **both topically and by oral application**, suggesting a global approach to maintain a healthy skin by treating it both internally and externally.

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