



LABORATOIRES
SÉROBIOLOGIQUES

Member of **cognis**

AGLYCAL® LS 8777

ANTI-GLYCATION

SKIN

GLYCATION AND DERMAL AGING

Glycation and action of the Reactive Oxygen Species (ROS)

Non-enzymatic glycation and attack by free radicals are two major and complementary mechanisms of dermal aging, characterized by damage of dermal extracellular matrix (DECM) macromolecules, such as collagen and hyaluronic acid. The DECM does not have any enzymatic system for protection and regulation against this damage.

Glycation of collagen

Reducing sugars bind slowly to the amino groups of collagen to form complexes (Maillard's reaction, or non-enzymatic glycosylation) in 3 steps:

- **1st:** formation of Schiff's bases (= early phase),
- **2nd:** Amadori's rearrangement: desoxyosones (= late phase) in presence of UV-A, O₂¹, Iron ++, formation of O₂⁻ and HO[•],
- **3rd:** formation of AGEs (Advanced Glycated Elements), terminal products of glycation.

Nonfunctional, glycated collagen is stored in the dermis, and leads to an inflammatory process that destroys the remaining healthy collagen.

The consequences of this process are cutaneous thinning and loss of elasticity.

The Anti-Glycation Concept

Some of the skin proteins damaged by glycation (Maillard) are: fibronectin, laminin and, in particular, elastin and the various types of collagen (I and IV). Furthermore, free radicals generated by Maillard's products induce a deterioration (depolymerization) of hyaluronic acid.

In normal young skin glycated proteins are eliminated; digestion by macrophages causes a restructuring of the dermis.

But this "renewing" capacity decreases with aging, causing an accumulation of glycated proteins. In simple words, glycation can be described as the accumulation of "bad sugars", bound on skin proteins like collagen.

To counteract this phenomenon, Laboratoires Sérobiologiques has developed AGLYCAL® LS 8777.

DEFINITION / COMPOSITION

AGLYCAL® LS 8777 is a unique, patented active ingredient, an association of active substances mainly of plant origin, especially selected and proven to inhibit the non-enzymatic glycation of proteins. In combination with its anti-free radicals activity, AGLYCAL® LS 8777 restores the elasticity and youth of the skin.

Main components:

AGLYCAL® LS 8777 is a complex of natural origin, containing:

- flavonoids of *Arctostaphylos uva ursi* (leaf),
- non-reducing saccharides, playing an indirect synergistic role in the anti-glycation activity.



Fig. 1A – *Arctostaphylos uva ursi*.

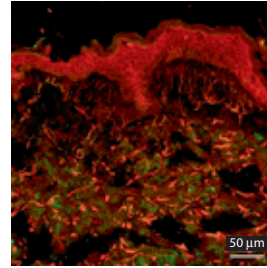


Fig. 1B – Young skin: presence of rare dermal deposits (green color).

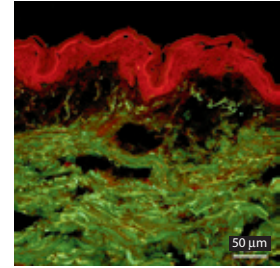


Fig. 1C – Old skin: presence of massive dermal deposits (green color).

SKIN BENEFITS

1. Anti-glycation of proteins, anti-aging, elasticity preservation.
2. Anti-free radical.
3. Protection against the fragmentation of dermal macromolecules.

COSMETIC USE

- Anti-age, anti-wrinkle, pro-elasticity care.
- Day and night care.
- Skin protective care.

DOSAGE / SOLUBILITY / MODE OF INCORPORATION

1. **Dose of use:** 0.75 to 1.5%.
2. **Solubility:** AGLYCAL® LS 8777 is hydro-soluble and insoluble in oils.
3. **Mode of incorporation:** AGLYCAL® LS 8777 has to be dissolved into 3 times its weight of water heated at 45 - 50°C. Do not heat over 60°C. Suitable between pH = 4.0 and pH = 6.0.

ANALYTICAL CHARACTERISTICS

1. **Aspect:** fine light-beige powder, with a weak odor.
2. **Specifications:** upon request.

TOLERANCE

Good.

EFFICACY

Test summaries overleaf.

STORAGE

In its original packaging, at 15 - 25°C.

INCI NAME

Mannitol (and) Cyclodextrin (and) Glycogen (and) *Arctostaphylos Uva Ursi* Leaf Extract.

MANUFACTURER

Laboratoires Sérobiologiques S.A.

ACTIVE INGREDIENT FOR COSMETOLOGY

EFFICACY TESTS

ANTI-ROS (REACTIVE OXYGEN SPECIES) AND ANTI-FREE RADICAL ACTIVITY

Aim

Determination of the anti-free radical activity of AGLYCAL® LS 8777 by using different test methods.

Protocol

The activity of AGLYCAL® LS 8777 was tested using:

- **Chemical test in tubo:** DPPH[•] / Fenton's reaction on desoxyribose (HO[•] radical),
- **Biochemical test in tubo:** Hypoxanthine / Xanthine-oxidase induced O₂^{-•}. Detection with luminol, luminol + microperoxidase or by NBT decrease.
- **Tests on cell cultures in vitro:** MRC5 human fibroblasts/activity against free radicals (DPPH[•] test) or against peroxides and lipo-peroxides (determination of GSH).

MRC5 cells in survival are treated with AGLYCAL® LS 8777 for 3 days, then the stabilized DPPH[•] and the GSH rate were determined.

Results

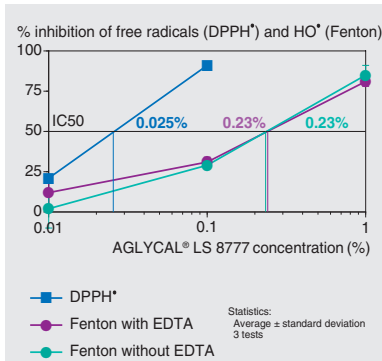


Fig. 2 – Efficacy against free radicals (DPPH[•]) and HO[•] radical (Fenton's reaction on desoxyribose).

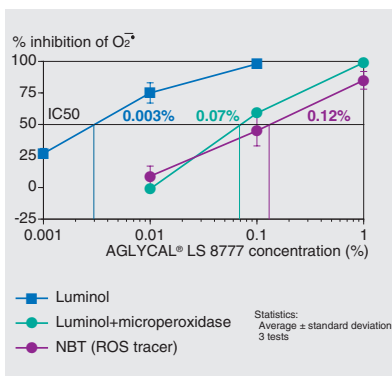


Fig. 3 – Anti O₂^{-•} (formed by Hypoxanthine/Xanthine-oxidase) effect, measured with different tracers.

NBT = Nitro Blue Tetrazolium

DMEM = Dulbecco's Minimum Essential Medium

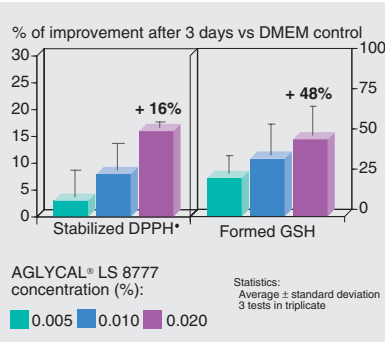


Fig. 4 – Test of activity on MRC5 human fibroblasts in survival in vitro by DPPH[•] test and GSH determination.

Conclusion

AGLYCAL® LS 8777 has a wide spectrum of anti-free radical activity, protecting against primary free radicals and ROS (O₂^{-•} and HO[•]). The endogenous defense system (GSH = reduced glutathione) is protected.

PROTECTION OF COLLAGEN I AND HYALURONIC ACID AGAINST THE DELECTERIOUS EFFECT OF REACTIVE OXYGEN SPECIES

Aim

Determination of the capacity of AGLYCAL® LS 8777 to protect collagen against free radicals.

Protocol

- HO[•] radicals were produced via xanthine oxidase in presence of hypoxanthine (Haber-Weiss's reaction) or by H₂O₂ in the presence of copper (Fenton's reaction). Xanthine oxidase in the presence of hypoxanthine forms O₂^{-•}; the latter is spontaneously transformed into H₂O₂ and O₂, and in the presence of trace concentrations of metals, H₂O₂ is cleaved into 2 HO[•] radicals.
- Singlet Oxygen (O₂¹) was produced by riboflavin in the presence of UV-A. IC50 (concentration to reach 50% inhibition) was determined. Collagen I and hyaluronic acid were incubated with these radicals and the extent of degradation was measured.

AGLYCAL® LS 8777 strongly decreased the degradation of collagen I by O₂¹ (IC50 ~ 0.02%) and the degradation of hyaluronic acid by HO[•] radical (IC50 ~ 0.04%) and by O₂¹ (IC50 ~ 0.95%).

Results

AGLYCAL® LS 8777 strongly decreased the degradation of collagen I by O₂¹ (IC50 ~ 0.02%) and the degradation of hyaluronic acid by HO[•] radical (IC50 ~ 0.04%) and by O₂¹ (IC50 ~ 0.95%).

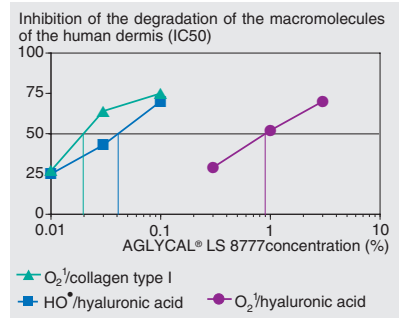


Fig. 5 – Protecting effect (IC50) against the degradation of the macromolecules of the dermis (collagen and hyaluronic acid) by the reactive oxygen species (HO[•] and O₂¹).

Conclusion

AGLYCAL® LS 8777 efficiently protects macromolecules of the dermis against attack by reactive oxygen species.

PROTECTION OF COLLAGEN TYPE I AGAINST NON-ENZYMATIC GLYCATION

Aim

Determination of the capacity of AGLYCAL® LS 8777 to protect collagen against glycation.

Protocol

Collagen I was incubated in a buffer medium (pH = 7.4) at 45°C for 21 days, in the presence of glucose (10 g/l) with (0.2%) or without albumin. At the end of incubation, the suspension was centrifuged and the fluorescence intensity (350/430 nm) was measured in the supernatant. The fluorescence increases with the concentration of collagen fragments.

Results

AGLYCAL® LS 8777 decreased the fluorescence of the supernatant in a dose-dependent effect:

- without albumin: IC50 = 0.93% (w/v),
- with albumin: IC50 = 0.78% (w/v).

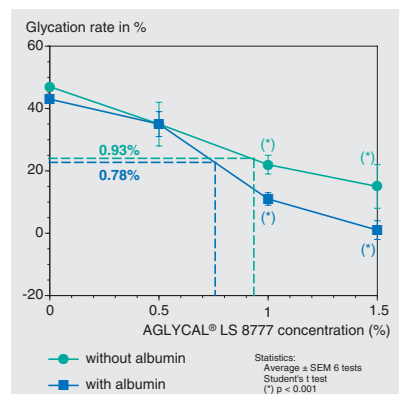


Fig. 6 – Demonstration of the dose-dependent anti-glycation capacity of AGLYCAL® LS 8777 on type I collagen.

Conclusion

AGLYCAL® LS 8777 has a strong capacity to decrease glycation of collagen I.