

EXSY-ARL®

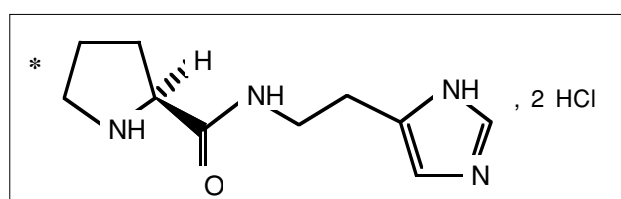
(formerly ARETYL)

EXSYMOL

Hydroglycolic solution (90:10 water:1,3-butanediol)
of polyglyoxaline AE (10%)*
INCI name : PROLINAMIDOETHYL IMIDAZOLE(and) BUTYLENE GLYCOL(and) WATER

Chemical Family

EXSY-ARL® is a hydroglycolic solution containing a synthetic pseudodipeptide of high stability and resistant to enzymatic hydrolysis.



Analytical composition

Prolyglyoxaline AE HCl	10.000 g
1,3-Butanediol	8.180 g
Sodium methyl paraben	0.145 g
Water	sq 100.000 g

Technical characteristics

limpid liquid, colorless
pH : about 5
density (20°C) : about 1
miscible to water, glycols and alcohols

Availability

1, 5 or 30 kg drums

Cosmetic use :

Skin and Sun care

- Preventive action :

EXSY-ARL® opposes protein cross-linking and improves the skin natural defense system.
(Anti-glycoxidation, anti-oxidation and chelation of transition metals).

- Repairing action :

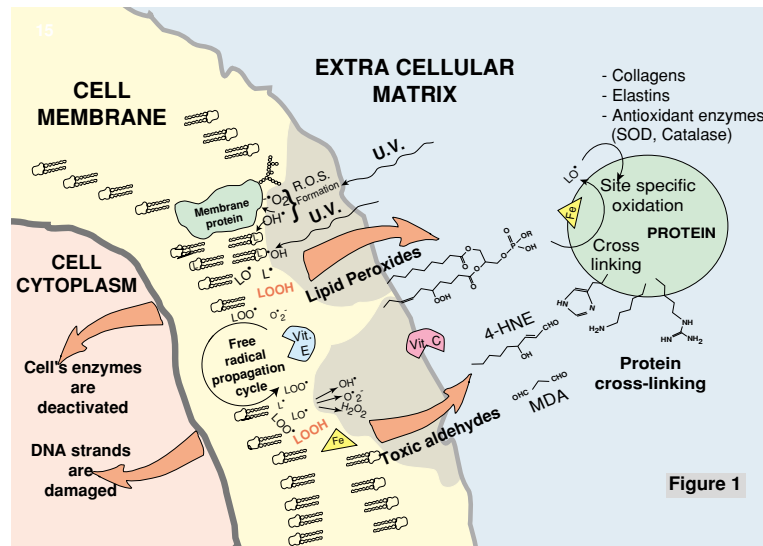
EXSY-ARL® detoxifies and protects cell membranes.
(Lipid peroxidase-like activity).

EXSY-ARL® is to be formulated in any anti-aging formulations
(creams, gels, lotions, milks, ...).

EXSY-ARL® may therefore be incorporated in day and/or night skin products,
sun and/or after-sun formulations, sensitive skin and acne prone skin products, ...

Deactivation of toxic aldehydes - Anti-pollution effect

Protecting effect against toxic aldehydes



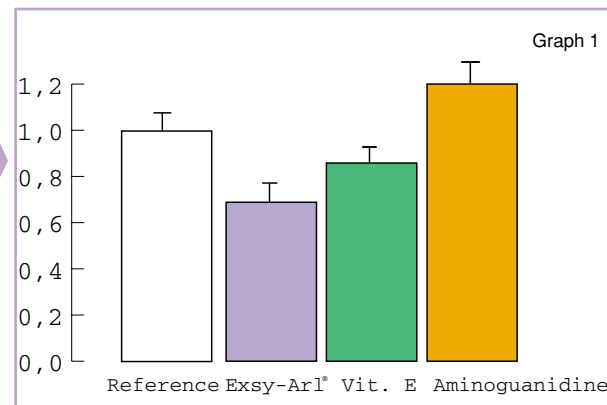
During an oxidative stress (e.g. UV irradiation, pollution...), peroxidation of biological membranes occurs. The phospholipids hydroperoxides thus formed are responsible for the propagation and amplification of the initial oxidative stress as they break down into free radicals (hydroxyl, lipo-peroxyl, ...) and amphiphilic toxic aldehydes. Among these, 4-hydroxynonenal (HNE) and malonaldehyde (MDA) have been identified and characterized as powerful protein cross-linking agents. These aldehydes may be regarded as toxic "second messengers" (Figure 1).

Figure 1

The "anti cross-linking effect" of **EXSY-ARL**® has been demonstrated *in vitro* by an immunoenzymatic assay (ELISA) capable of recognizing glucosone-induced cross-linked collagen.

The efficiency of **EXSY-ARL**® was compared to that of vitamin E and that of aminoguanidine (graph 1).

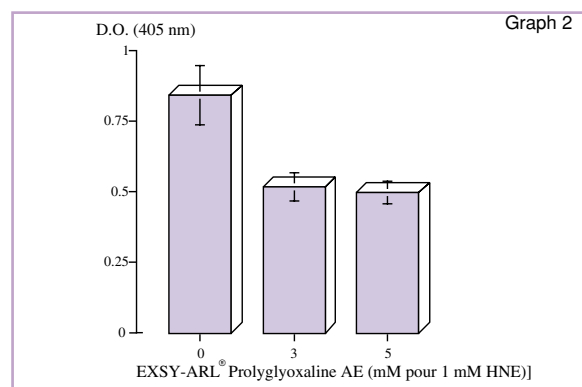
EXSY-ARL® strongly deactivates toxic "second messengers" (toxic aldehydes).



Graph 1

A similar test carried out on α -crystallin, a heat shock or chaperone-like protein, has shown similar protecting properties against HNE-induced protein degradation (graph 2).

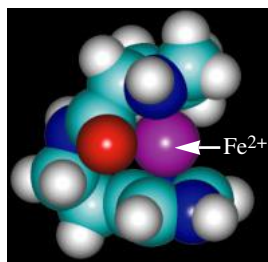
Therefore its protection by **EXSY-ARL**® can be regarded as a protection of the skin natural defense system.



Graph 2

Transition metals chelating properties

A reconstructed 3D image, based on a computer aided calculation, showed that prolyglyoxaline AE chooses preferably a "claw-like" conformation, creating a site in which transition metals (picture besides). This property endows this biomimetic pseudodipeptide with a capacity to oppose the iron toxicity by stabilizing it and impeding to fix onto the biological molecules ("site-specific oxidation"), without inhibiting the biological useful process that also need iron (**EXSY-ARL**® does not inhibit catalase activity even at high concentration).

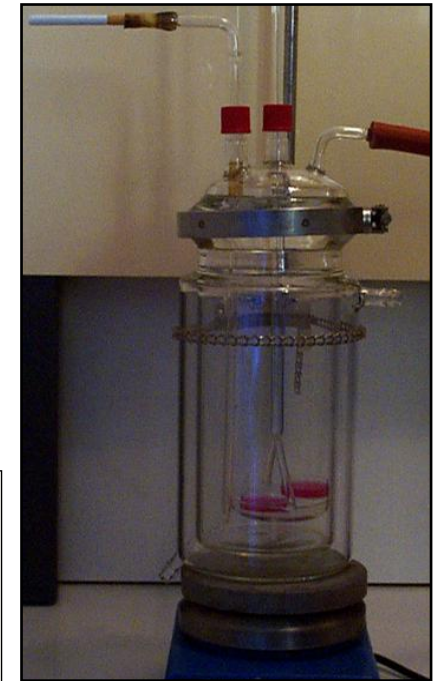


Anti-pollution effect

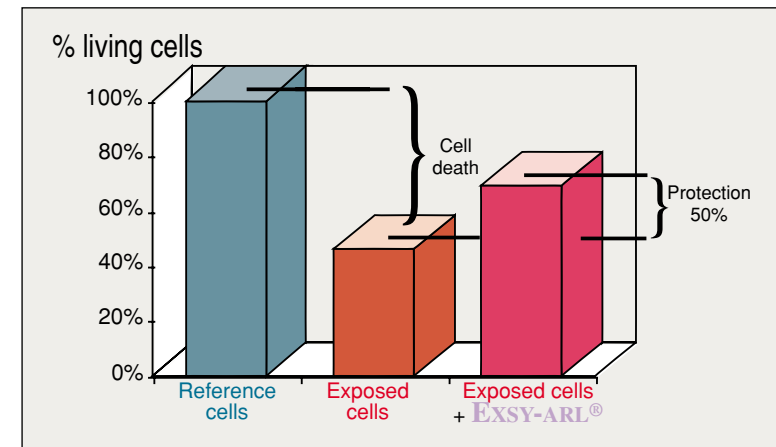
One of the most frequent stress of our everyday life is that related to urban environment and pollution. Pollution is constituted of several toxic materials such as toxic aldehydes, free radicals, heavy metals...

In the test, presented herein, the effect of cigarette's smoke has been selected to be studied on some particular cells of the epiderm. Actually, cigarette's smoke is considered as a very good model for atmospheric pollution.

Keratinocytes are submitted to a controlled atmosphere containing cigarette's smoke and inducing 50% of cell death. At the same time, other cells are submitted to the same treatment but their culture medium had been previously enriched with **EXSY-ARL**®. In these conditions, 75% of the cells survived.

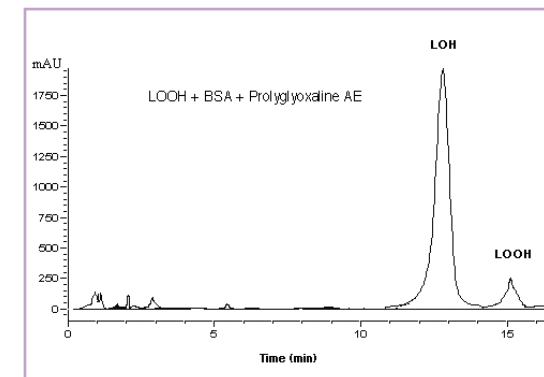


The anti oxidant activities of **EXSY-ARL**® are confirmed with this type of test. These properties can be further adapted to the actual anti pollution effect, considered as a major stress of modern life.

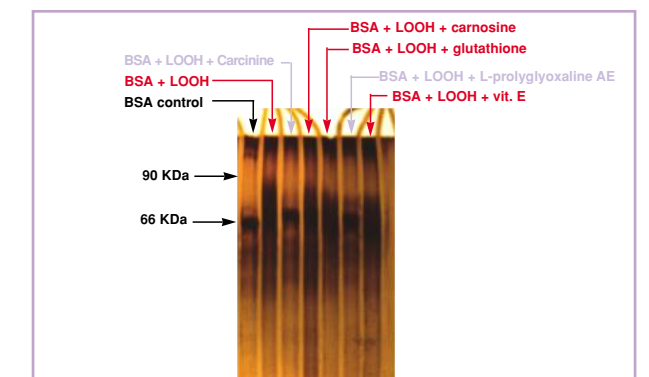


Reduction of fatty acids hydroperoxides

EXSY-ARL®, as a pseudodipeptide containing an imidazole ring, is able to reduce the fatty acids hydroperoxides (LOOH) into non toxic alcohols (LOH) (graph 3). This activity can be evidenced *in vitro*, by measuring the capacity of the pseudodipeptide to prevent the proteins from oxidative cross-linking (graph 4).



Graph 3 : HPLC Analysis of BSA submitted to LOOH in presence of prolyglyoxaline AE (**EXSY-ARL**®)



Graph 4 : Electrophoresis (SDS Page) of BSA submitted to LOOH

Tolerance study

The tests performed both *in vitro* and *in vivo* indicate that the product is neither toxic nor irritant. These tests consist in studying :

1. *In vitro* (alternative methods) :
 - ocular irritation on fibroblasts culture isolated from rabbit cornea.
 - cutaneous irritation on reconstituted epidermis.
2. *In vivo* (human volunteers) :
 - photo-sensitization on healthy human volunteers (phototoxicity and photo-allergy).

Formulation

EXSY-ARL® is a perfectly stable hydroglycolic solution (90:10 water: 1,3-butanediol). The product can be formulated in the aqueous phase without restriction nor constrain.
The suggested use level varies from 0.5 to 1.5%.

Existing Studies

Technical data

*

Anti-oxidant activity :

- anti free radical activity (scavenging effect).
- reducing activity (lipid peroxidase-like affect).

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Anti-oxidant activity on cell culture

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Cytostimulating activity on cell culture

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Toxic aldehydes and Pseudodipeptides
(Protection against proteins cross-linking)

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Anti-pollution activity

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Tolerances

(alternative methods & study on healthy human volunteers)