EXAGE®

Antidote against glycotoxin-induced aging

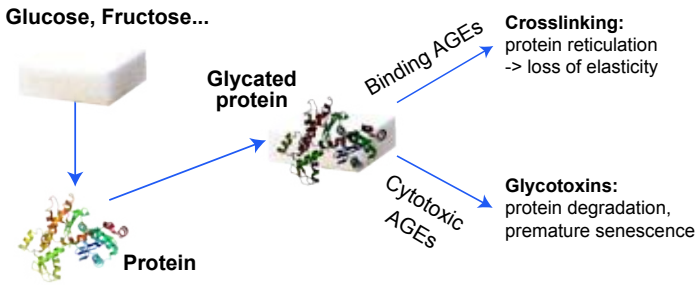
GLYCODETOXIFICATION
CELL DETOXIFICATION
ANTI-METABOLIC TIREDNESS
ANTI-AGING: ANTI-SLACKENING AND ANTI-WRINKLE
ANTI-SKIN POLLUTION
ANTI POISON'AGING

EXSYMOL
MONACO

EXAGE®

GLYCATION

Glycation (also known as Maillard's reaction) is the reaction between sugars and the amine moiety of protein-constituting amino acids. Exsymol has shown that, through the transglycation process, it is possible to reverse this reaction before it becomes irreversible. There are two possible outcomes for glycated proteins (AGEs): reticulation (or cross-linking) to another protein, and/or oxidative degradation into glycotoxins (cytotoxic AGEs).
So far, the cosmetic industry only focused on the prevention against reticulation, especially for structure proteins such as collagen and elastin fibers, since this process is **responsible for the loss of elasticity and for the whole skin architecture collapse.**



GLYCOTOXINS

Glycotoxins are most reactive and toxic AGEs. They are the end-products of glycated proteins oxidative degradation.
Contrarily to the glycation process, glycotoxins have a close to instant noxious effect on their protein targets.
While fructose and glucose are the two main responsible for the glycation process, methylglyoxal (MGO) and glyoxal (GO) are the most common glycotoxins.

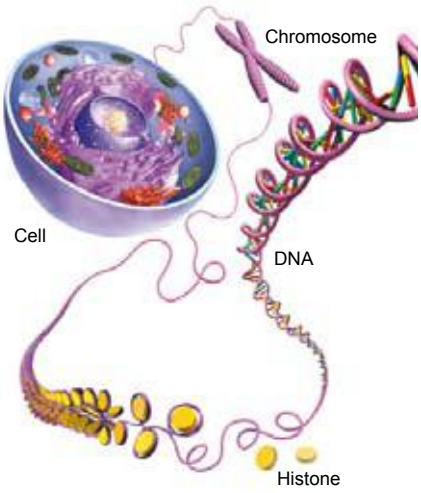
A FEW EXAMPLES OF INTRACELLULAR PROTEINS TARGETED BY GLYCOTOXINS

HISTONES:

Histones are the main proteinic constituents of chromosomes as the DNA is coiled around these proteins.
Histones are involved in DNA compaction into nucleosomes and are responsible for DNA availability for the transcription and replication processes. Because histones are favored targets for the glycation process as they are rich in arginine (an amino acid rich in amine moieties), there is a risk of histone loss of function and DNA alteration.
Histone alterations contribute to the premature aging process, especially because of the apparition of a senescence phenotype, which is due to DNA structural and functional disorganization.

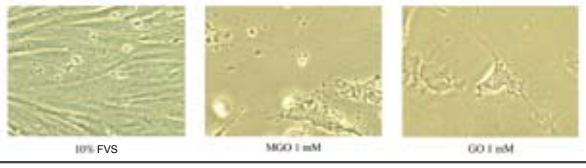
VIMENTINE:

Vimentine is one of the major constituents of cell cytoskeleton.
Vimentine is responsible for organelle positioning and anchorage within cells. On top of granting cells with flexibility, vimentine allows intracellular transportation of proteins.
Because vimentine is rich in lysine (amino acid rich in amine moiety), it is a favored target for glycotoxins which will cause a redistribution of vimentine into aggresomes. These alterations contribute to the **skin premature aging process**, especially because of the loss of interactions between essential organelles.



CELL POISONING: IMPACT OF GLYCOTOXINS ON CELL METABOLISM

Cell intoxication, similarly to **poisoning** contributes to a loss of homeostasis which **may lead to premature senescence and cell death**.
Histological studies have shown how toxic the most common glycotoxins (MGO and GO) are and fibroblasts exposed to glycotoxins quickly lose their spread shape and die.



DESIGN OF A GLOBAL ANTI-GLYCATION COMPOUND: EXAGE

Many studies have shown that classical anti-glycation compounds (such as carnosine) are not capable of neutralizing glycotoxins. As a result, EXSYMOL designed an anti-glycation compound capable of scavenging sugars, of performing the transglycation process (one of our latest technology) and, most of all, capable of detoxifying extra- and intra-cellular compartments from glycotoxins: EXAGE.

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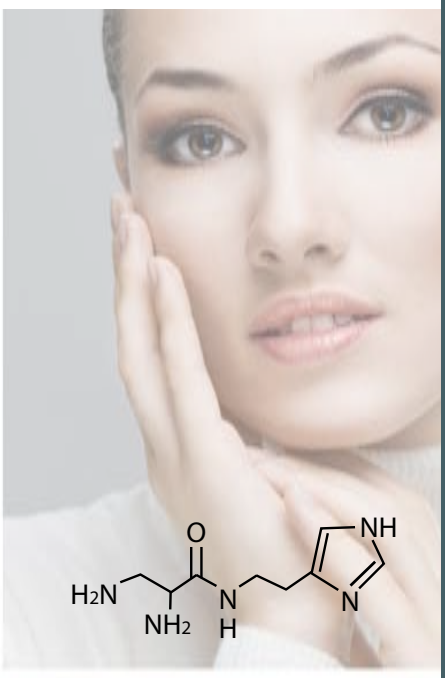

EXAGE®

INCI name: Imidazolylethyl Diaminopropanamide HCl

EXAGE is a 10% dilution of DAPHIS (INCI name: Imidazolylethyl Diaminopropanamide HCl)

EXAGE *provides an innovative and essential approach against glycation.*
While the cosmetic industry is focused on the preservation of structure proteins' quality, Exsymol strikes back at the glycation end products. Underestimated for a long time, glycotoxins are one of the main negative factors responsible for the skin premature aging.
EXAGE *is an antidote against the glycotoxins responsible for cell metabolism intoxication.*

Levels anti-glycation activity
-Sugar scavenger
-Reverse glycation
-Prevention of AGE formation
-AGE detoxification

Tri-compartmental global protection
-Proteins from the extracellular matrix
-Intracellular proteins
-Intranuclear proteins

SKIN BENEFITS

Sugar scavenging
Deglycation
Fast AGE scavenging
Anti-skin architecture collapse (loss of elasticity)
Anti-metabolism alterations (loss of viability)

COSMETIC APPLICATIONS

Face and body
Anti-aging
Skin glow
Protection
Anti-glycation
Anti-deep wrinkle

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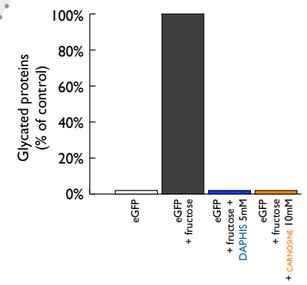
GLYCATION, GLYCOTOXINS AND DETOX'AGES TRI-COMPARTIMENTAL

GLUCOSE, **FRUCTOSE...**

+

PROTEIN
Collagen, histone, elastin, enzyme...

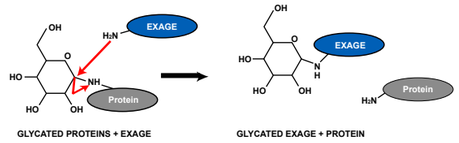
PREVENTION
Sugar scavenging



Because of the glycation process, fructose (one of the main sugars responsible for the glycation process) induces a reticulation of our model protein (eGFP).

EXAGE's scavenging ability completely prevents protein reticulation hence maintaining 100% of protein functions.

REPARATION
Deglycation

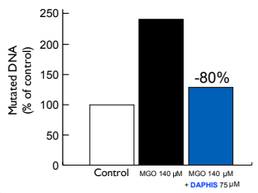


EXAGE is one of these revolutionary anti-glycation compounds capable of substituting themselves to the glycated protein.

Hence, by reversing the glycation process in its early stage, EXAGE ensure an optimal protein function.

DETOXIFICATION
Quick glycotoxin deactivation

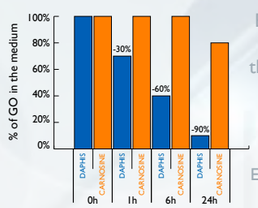
EXAGE's quick neutralization of glycotoxins together with its end products' lack of toxicity makes it very efficient at preventing premature senescence and/or cell death.



This study shows that glycotoxins have very high mutagenicity (+140% of mutated DNA).

Because of a treatment with EXAGE, the amount of MGO-induced DNA mutations is decreased by 80%.

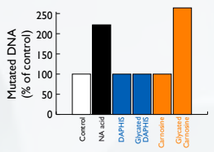
Kinetic of detoxification



Because of glycotoxins' toxicity and their high ability to diffuse throughout extracellular, cellular and nuclear compartments, it is mandatory to quickly detoxify skin cells.

EXAGE **neutralizes about 50% of glycotoxins after only 3h and 90% after 24h.**

Detoxification end products' lack of toxicity



A detoxifier may also turn into an AGE after scavenging a glycotoxin.

It is therefore mandatory to prove the lack of toxicity of EXAGE-generated detoxification end products.

Skin aging

Loss of enzymatic activity

Loss of elasticity and structure protein collapse

CROSS-LINKING

Binding AGEs

GLYCATED PROTEIN
Dicarbonyled protein

Cytotoxic AGEs

GLYCOTOXINS

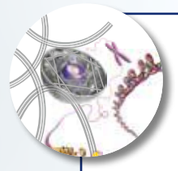
GO and MGO are the most common glycotoxins. MGO is a marker of interest in patients affected with diabetes.

Skin cell metabolism slow down

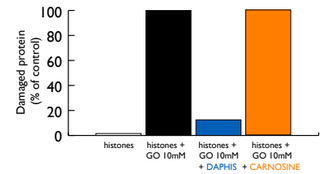
Premature cell senescence

Loss of skin elasticity

Skin aging

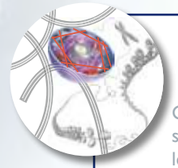


PROTECTION OF NUCLEAR PROTEINS



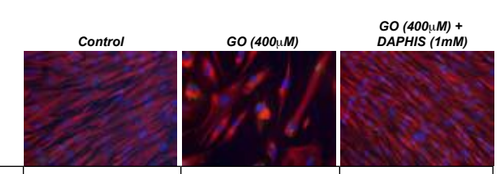
A fluorescence study has shown that histones (nuclear proteins in direct contact with DNA) are very sensitive to glycotoxins.

Exage reduces the risks of DNA disorganization and mutation by 75%. Such DNA impairment may lead to:
-cell metabolism slow down
-premature senescence
-premature skin aging



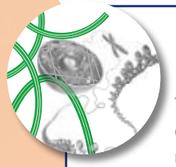
PROTECTION OF INTRACELLULAR PROTEINS

Glycotoxins have a very noxious effect on vimentin which is involved in cell structure. Glycotoxin-induced glycation causes vimentin aggregation hence leading to cell death.



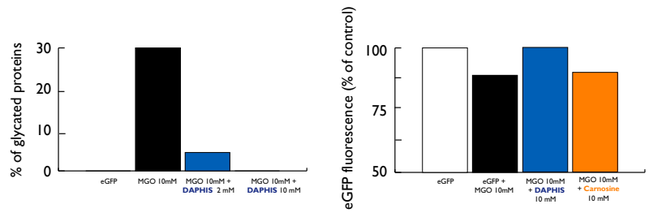
	Control	GO (400µM)	GO (400µM) + DAPHIS (1mM)
Quality of the vimentin network	+	-	+
AGE formation	0	+	0
Cell viability	+	-	+

EXAGE's detoxification activity protects skin cell's architecture and therefore ensure their survival.



PROTECTION OF THE EXTRA CELLULAR MATRIX

Thanks to a protein model synthesized in EXSYMOL's biotech labs : eGFP, we monitored the glycation-induced protein degradation and its related AGE production.



EXAGE's detoxification activity completely prevents protein glycation. By ensuring structure proteins' function, EXAGE efficiently opposes skin architecture collapse.

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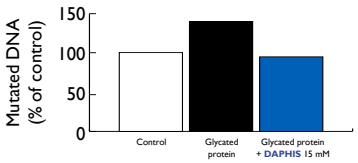
EXAGE'S COSMETIC BENEFITS

DNA PROTECTION

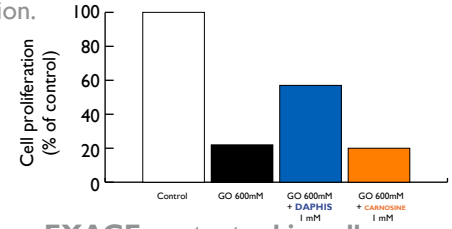
Glycated proteins produce glycotoxins which are responsible for DNA alterations.



EXAGE protects DNA from glycotoxin's mutagenic effects.

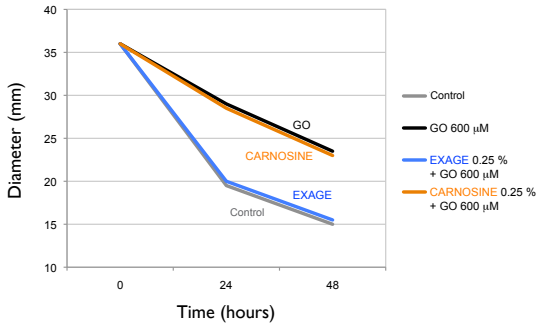
ANTI-POISON'AGING: CELL PROTECTION

AGE exposure leads a dramatic drop in skin cell proliferation.



EXAGE protects skin cells from AGE-induced proliferation inhibition.

RECOVERING OF SKIN ELASTICITY



This study on collagen lattice shows that AGEs are responsible for a loss of fibroblast's contractile ability.

EXAGE's ability to detoxify the skin from glycotoxins leads to a full recovery of fibroblast's contractile capacities.

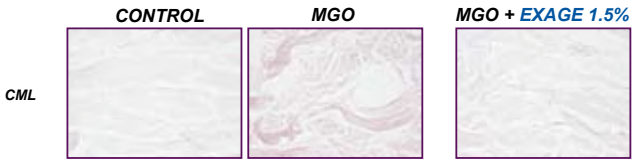
Contrarily, Carnosine is not capable of detoxifying skin from AGEs and thus, does not have any effect on fibroblasts' contractile ability.

By efficiently detoxifying skin from glycotoxins, EXAGE completely restores its elastic properties.

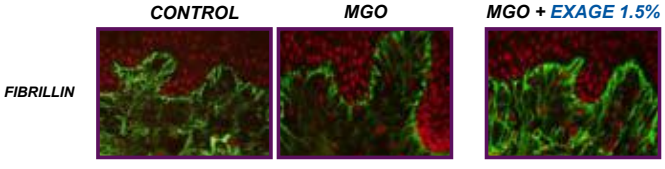
SKIN PROTECTION – EXPLANTS

A study on human skin explants confirmed all benefits provided by a treatment with EXAGE (1.5%).

Glycotoxin are responsible for structure protein glycation. The model below showed that these AGEs cause collagen aggregation. EXAGE is capable of protecting the collagen from this aggregation hence ensuring its elastic architecture.



EXAGE prevents AGE formation (marked in pale purple by Carboxymethyl-lysine specific marker) within the dermis.



Exage protects fibrillin, a protein involved the dermal epidermal junction's structure.

Exage protects the skin from an architecture collapse due to glycotoxin-induced structure protein reticulation.

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EXAGE®

INCI name: Imidazolylethyl Diaminopropanamide HCl

TECHNICAL CHARACTERISTICS

ANALYTICAL COMPOSITION

DAPHIS (IMIDAZOLYLETHYL DIAMINOPROPANAMIDE HCL)	10%
Methyl-2 propanediol-1,3-diol	20%
Water (sq)	100%

PHYSICO-CHEMICAL CHARACTERISTICS

Limpid to slightly opalescent liquid
Colorless to pale yellow
pH ≈ 4,5
Density at 20°C ≈ 1.0
Miscible with water

PRESERVATIVES

No preservative

TOLERANCE AND TOXICITY STUDIES

EXAGE is perfectly tolerated. Tolerance and toxicity studies were performed using both *in vitro* (cell culture and reconstructed epidermis) and *in vivo* (human volunteers) methods

FORMULATION

Advised doses: 0.5 to 1.5%

AVAILABILITIES

EXAGE is available in 1, 5 and 30kg drums

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