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# Collrepair™ DG – Anti-Ageing Active Ingredient Reverses 20 Years of Skin Glycation

## ■ Introduction

Glycation is one of the major causes of skin ageing. It is the result of the typical covalent bonding of a protein or lipid molecule with a sugar molecule such as glucose, and the first step in the evolution of dreaded advanced glycation end products (AGEs), which are produced through a complex series of biochemical reactions. AGEs accumulate over time: Slowly and irreversibly, glycation damages the structure of the cells and the extracellular matrix (ECM), and thus the structure of the skin. As a result, the skin loses its elasticity and re-

siliency, the skin tone is altered through yellowing, and surface wrinkles start to appear.

A lot of research has been aimed at preventing glycation and there are a number of active ingredients which effectively protect against it, including aminoguanidine, Carnosine, Collguard™ and Arganyl™. But in the past decades, little progress has been made in finding ways to reverse the process and bring about a decrease in the skin's total glycation level.

Now a breakthrough has been made in matrix fiber management: With their new active ingredient Collrepair™ DG,

experts from BASF Beauty Care Solutions have found a way to reverse 20 years of glycation within 4 months' time.

## ■ Product Definition

Collrepair™ DG is a synergistic, aqueous complex of salvia miltiorrhiza leaf extract and niacin or vitamin B3 (INCI: Water (and) Niacin (and) Caprylyl Glycol (and) Hexylene Glycol (and) Xanthan Gum (and) Salvia Miltiorrhiza Leaf Extract).

Niacin was selected for testing because of its chemical structure and nucleophilic properties, which resemble those of a well-known AGE breaker, alagebrium chloride (ALT-711) (1). Niacin helps to break down blood sugar and convert it into energy. High doses of niacin can also reduce cholesterol levels, triglyceride levels, and cardiovascular risks. Salvia miltiorrhiza is also known as »red sage«, or »Chinese sage«. In traditional Chinese medicine, it is highly valued for its positive effect on cardiovascular disorders such as atherosclerosis.

## ■ Solutions Up Close: Formulation Examples

See Table 1.

## ■ Product Studies

Efficacy Demonstrated *In Vitro* and *In Vivo*

The deglycating efficacy of Collrepair™ DG has been proven in both intracel-

## Abstract

**B**ASF's Collrepair™ DG is a revolutionary breakthrough for deglycation and the removal of advanced glycated end products (AGEs). AGEs continue to form as we age and accumulate over time, but Collrepair™ DG is able to break glycated crosslinkages both intracellularly in fibroblasts and extracellularly within the skin. Collrepair™ is clinically proven to remove approximately 20 years worth of AGE accumulation and approximately 17 years of sallowness (yellowing), and improve skin elasticity. Collrepair™ DG is soluble in both water and glycol and is suitable for use in creams, lotions, and tonics.

lular and extracellular proteins, and demonstrated *in tubo*, *in vitro* and *in vivo*.

**Effect on Glycated Collagen *In Tubo***

The ability of Collrepair™ DG to decrease extracellular AGEs, i.e. N<sub>(ε)</sub>-(carboxymethyl)lysine (CML), a common type of AGE in human skin, was first demonstrated in a solution of isolated human collagen. The collagen was extracted from human skin (obtained by biopsy) and glycated *in tubo* by adding ribose. After 3 weeks of incubation at 30 °C, the degree of collagen glycation, i.e. the presence of CML adducts, was evidenced by an increase in fluorescence at 355exc/430em. (Fig. 1)

In 24 h at 30 °C, in concentrations of 0.1 % to 0.5 %, the complex significantly decreased the amount of AGEs, i.e. CML adducts, with a maximum efficacy of 0.5 % leading to a decrease by 30%. As the test was conducted in a solution of isolated collagen, without any cellular repair or detoxification systems,

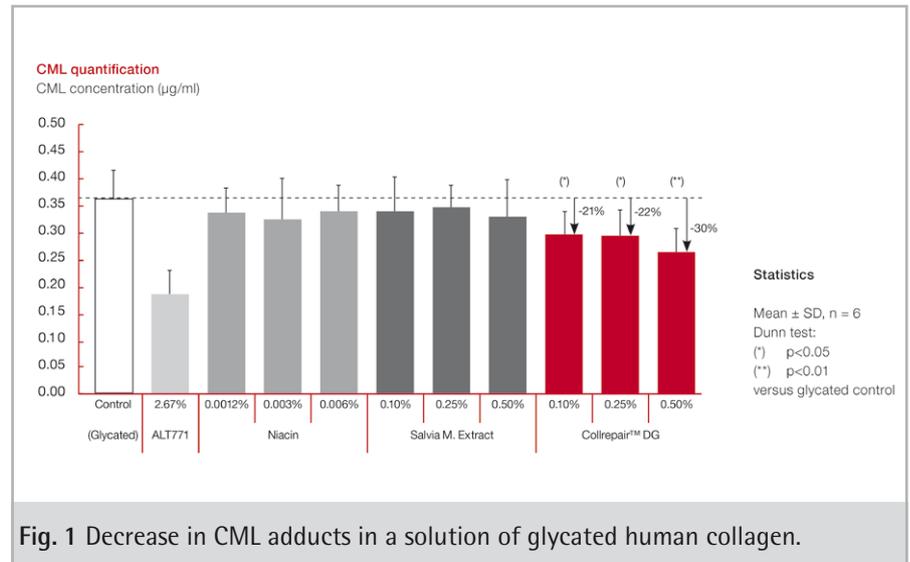


Fig. 1 Decrease in CML adducts in a solution of glycated human collagen.

the mode of action had to be an AGE-breaking one. A similar mechanism had already been described for alagebrium chloride (ALT-711), which was used as a positive control for the AGE-breaking effect, at 2.67 % (500 µM). The efficacy of Collrepair™ DG shows the synergistic

effect of salvia miltiorrhiza and niacin when used in combination; however, salvia miltiorrhiza extract and niacin had no significant effect when tested separately.

**Effect on Glycated Collagen *In Vitro***

The intracellular effect of Collrepair™ DG on a glycated fibroblast monolayer culture was assessed *in vitro*. Glyoxal was used as a glycyating agent (200 µM for 7 days).

Two effects were seen: First, a decrease in CML accumulation in fibroblasts and, second, a normalization of vimentin distribution in fibroblasts versus the glycated control.

Compared to the untreated control, 7 days of Collrepair™ DG 0.25 % significantly reduced the volume of accumulated AGEs (CML) (85%). In addition, it repaired the effects of glycation on vimentin distribution, as demonstrated by immune-fluorescent visualization (Fig. 2). In glycated fibroblasts, the protein is concentrated in the perinuclear area. Fibroblasts treated with Collrepair™ DG returned to a regular vimentin distribution, allowing the cells to regain their fused shape and therefore their functionality.

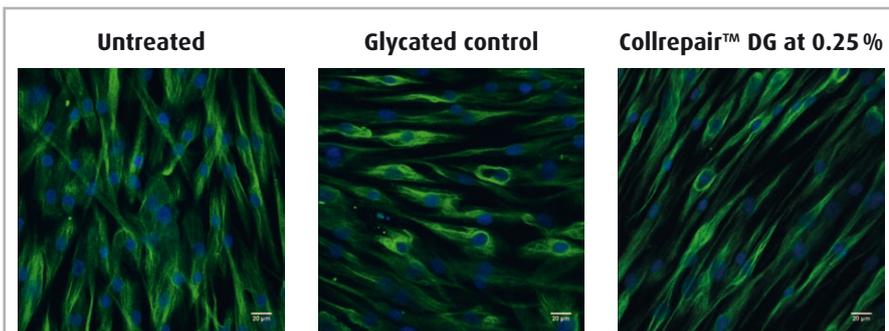
***In Vitro* Deglycation Conclusion**

**Extracellular Deglycation Proven**

- Significant decrease of glycation marker CML in human collagen

Ingredient	INCI/Chemistry	%
Emulgade® SE-PF	Glyceryl Stearate, Cetearth-20, Cetearth-12, Cetearyl Alcohol, Cetyl Palmitate	5.00
Lanette® 22	Behenyl Alcohol	2.00
Cegesoft® C24	Ethylhexyl Palmitate	5.00
Cetiol® PGL	Hexyldecanol, Hexyldecyl Laurate	3.00
Cetiol® OE	Dicaprylyl Ether	3.00
Xiameter PMX-200 Silicone Fluid 50 CS (Dow Corning)	Dimethicone	1.00
Cosmedia® SP	Sodium Polyacrylate	0.80
Water	Aqua	Sqf 100
Elestab® 388	Propylene Glycol, Phenoxyethanol, Chlorphenesin, Methylparaben	2.50
Glycerine (Oleon)	Glycerin	3.00
Keltrol CGT (CP Kelco)	Xanthan gum	0.20
Eumulgin® SG	Sodium Stearoyl glutamate	0.40
Collrepair™ DG	see article	3.00

Table 1 Example formulation using Collrepair™ DG. Collrepair™ DG is soluble in water and glycol. The recommended dose is from 3 to 5 %. Collrepair™ DG is colored in alkaline environment. This coloration is not reversible – to avoid coloration, it is recommended to adjust 4<pH<5.5, and use a chelant agent like EDTA with an anti-oxidant.



**Fig. 2** Normalization of vimentin distribution with Collrepair™ DG versus glycated control. Immunofluorescence staining of vimentin (green); nuclei in blue, scale bar 20 µm; anti-vimentin monoclonal antibodies followed by Alexa fluor™ 633 secondary antibodies; nuclei were counterstained using DAPI-containing mounting medium.

Over several months of application, the active ingredient steadily decreased accumulated AGEs, causing a significant reduction of 4% after four months (Fig. 3). This decrease represents half of the difference naturally observed between 2 groups of individuals separated by 40 years. Collrepair™ DG reversed 20 years of glycation in only 4 months.

**Effect on Skin Yellowing**

Skin yellowing is linked to AGEs accumulation, and was evaluated by measuring the b parameter (yellow component) via chromametry and image analysis. To rule out tan-related skin discoloration, the trial was conducted in winter.

Over a period of two to four months, Collrepair™ DG showed a continuous and significant reduction in skin yellowing against the baseline (Fig. 4). After four months, yellowing had faded by 8.1% with Collrepair™ DG, versus 6.8% with a placebo.

**Effect on Elastic Recovery**

The improvement in the skin's biomechanical properties i.e. skin elastic recovery was evaluated during a second, month-long clinical study with Collrepair™ DG 5%, using a cutometer. The formulation was tested on the

**Intracellular Deglycation Proven**

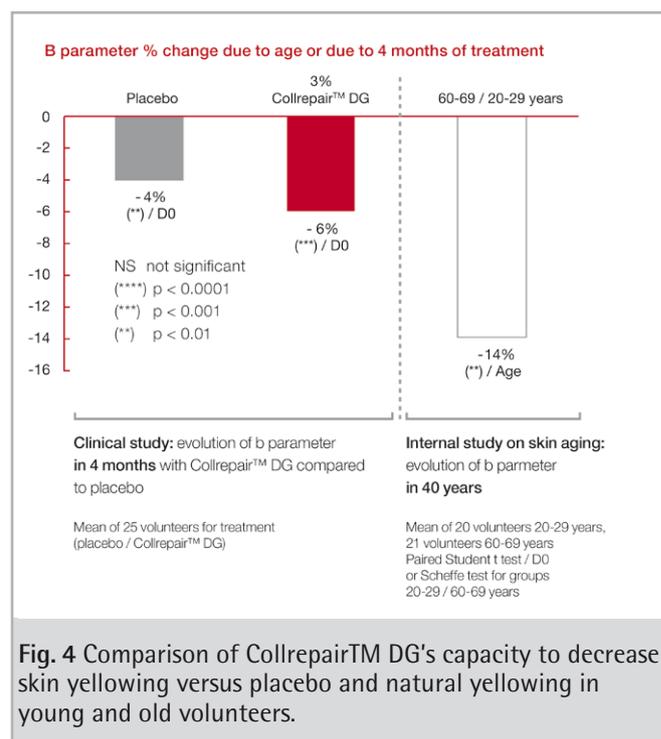
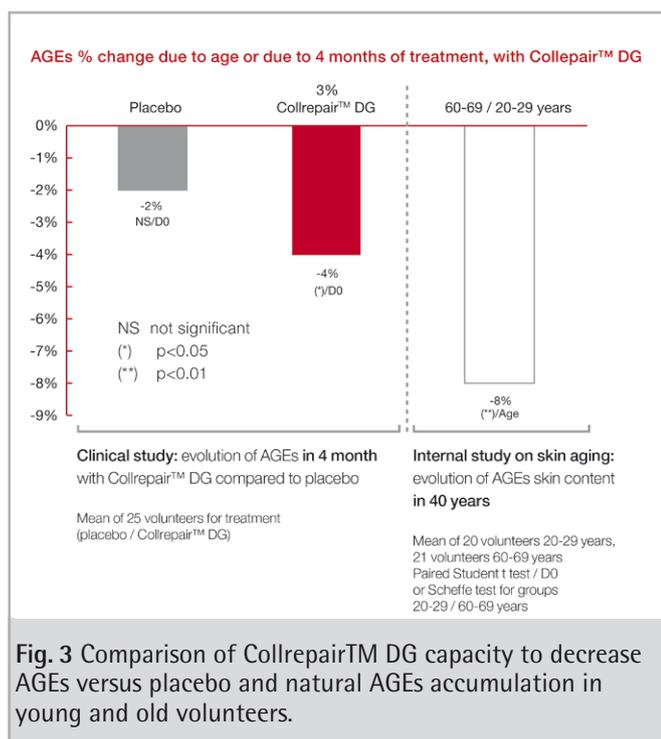
- Significant decrease of glycation marker CML in a fibroblasts culture
- Deglycation of vimentin (intracellular cytoskeleton morphology)

surement\* revealed an approximately 8% difference between the older and younger test groups.

In a second study, the efficacy of Collrepair™ DG was assessed. Over four months, twice a day, Collrepair™ DG at 3% was applied on one side of the face, against a placebo formula on the opposite side of the face of 27 Caucasian female test subjects ranging from 45 to 60 years old and with dull complexions. In addition to the decrease in cross-linked AGEs in collagen, skin tone improvement was also assessed.

**In Vivo Efficacy**

In a previous internal study on skin aging, evolution of AGEs in the skin had been assessed. Test subjects had been divided into two groups, 40 years apart (20-29 and 60-69 years old). The mea-



\* The AGEs accumulated in the skin were quantified using a spectrofluorimeter LS 55 equipped with a fiber optic probe (Perkin Elmer) (exc/em 370nm / 460-500nm). AGE fluorescence was normalized with skin autofluorescence (em 380-400nm).

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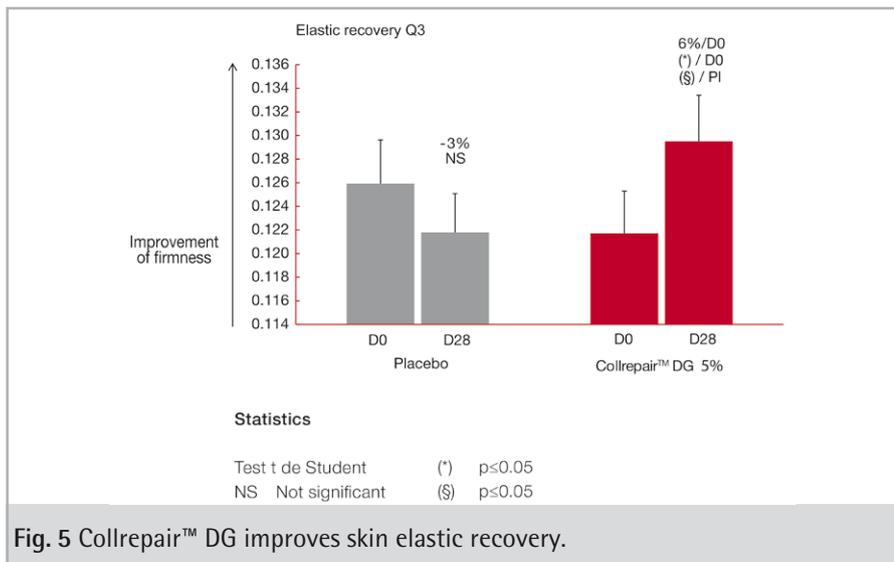


Fig. 5 Collrepar™ DG improves skin elastic recovery.

skin yellowing, restores a healthy skin tone, and recovers skin firmness. Collrepar™ DG is soluble in both water and glycol and suitable for use in creams, lotions, and tonics. With Collrepar™ DG, BASF Beauty Creations has entered a new era in the approach to managing skin ageing.

Full test results upon request – for customers.

Reference

(1) Extracellular glycation crosslinks: prospects for removal. *Furber JD. Rejuvenation Res. 2006 Summer;9(2):274-8.*

arms of 39 Caucasian female test subjects (45 to 60 years old), against a placebo (Fig. 5). In just 28 days, the active ingredient significantly increased the skin's elastic recovery – outperforming the placebo by 6%.

In Vivo Deglycation Conclusion

- Significant reduction of AGEs within the skin (clinically proven and measurable deglycation activity)
- Reduction of yellow skin tone (sallow-ness) by 10% in volunteers (clinically proven improvement in skin tone)

- Significant improvement of skin elastic recovery (clinically proven to restore elasticity)

Conclusion

Collrepar™ DG is the first active ingredient in the cosmetics field to reverse both intracellular and extracellular glycation with proven, significant results both *in vitro* and *in vivo* versus a placebo. It breaks down AGEs and reverses the equivalent of 20 years of glycation within just four months. In addition, it reverses glycation-related

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