

**PROTELAN AGL 95**  
**PROTELAN AGL 95/C**

*Acylglutamates*  
*the reason of a choice*

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## I. INTRODUCTION

Speaking of acylaminoacids involves a brief look at the substrata where they act, that means skin and hair.

Skin is comprised of two distinct units: epidermis and dermis (1).

Epidermis, the outer segment, has four basic layers.

These various layers represent different stages of cells differentiation, beginning with the stratum basale located just above the dermo-epidermal junction.

Above stratum basale there is the stratum spinosum where the cells are characterized by a spiny appearance and presence of desmosomes and then we find the stratum granulosum with the occurrence of intracellular granules.

In some regions of the body it is possible to have a thin homogeneous stratum lucidum and outermost we find the stratum corneum, that means the horny layer (2).

Obviously the most important barrier function is localized in the outer layer of the epidermis, the horny layer; this function is partially mechanical and partially physical in character and its prime purpose is protection from drying out and reduction of transcutaneous water loss. The horny layer is composed of about 20 layers of metabolically inactive cells, the protein-enriched lipid-depleted corneocytes, embedded in an extracellular matrix of lamellar double layers of lipids. These cells thereby endow the horny layer with physical and chemical stability and can be compared to the bricks in a wall (1).

The process of synthesis of the horny layer from its two structural elements (protein-containing cells and lipid lamellae in the intercellular space) let us understand the mechanism of action of topic formulations.

The stepwise differentiation from living keratinocytes to dead corneocytes is accompanied by significant changes in function and properties and involves many processes.

The cells lose their ability to divide, begin to produce new, differentiation-specific keratins that aggregate into bundles and thus can play a decisive role in the stability and rigidity of the horny layer itself (3).

During the keratinization process lysosomal enzymes disrupt all intracellular organelles, such as cell nucleus, mitochondria and macromolecular components.

Nucleic acids and the no longer required proteins are not synthesized anymore and lipid metabolism changes direction. A chemically very resistant protein membrane, the cornified envelop, is synthesized under the metamorphosing plasma membrane and covalent and associated lipids bind to its outside. Thus, the corneocyte consists of a cornified envelope stuffed full of keratin bundles (3).

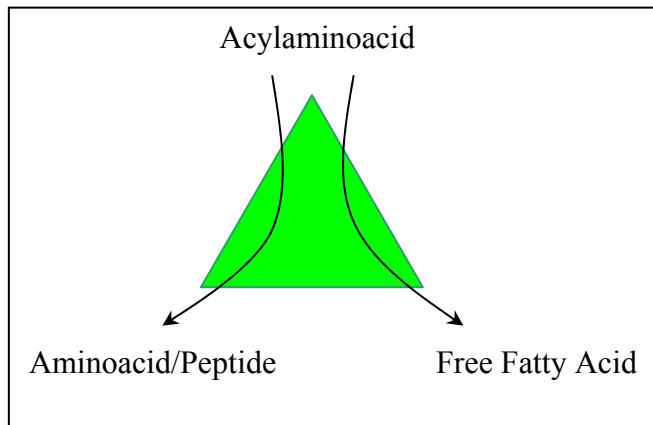
The lipids of the mortar and the precursor lipids are synthesized in the cells of the stratum spinosum and stratum granulosum and stored as intracellular, lamellar granules named Odland bodies (3).

These lamellar bodies are already detectable in the upper stratum spinosum and form vesicles with lipid lamellae arranged in parallel. Such lamellar bodies constitute another form of lipid secretion into the extracellular space alongside lipoproteins, whose synthesis is limited to certain cells. During this process a big quantity of enzymes is also exocitaded in the extracellular environment.

Examples of these enzymes are: acid lipase, phospholipase, carboxipeptidase, acid phosphatase and so on.

That means that if we apply an acylated aminoacid on the skin we are able to obtain the two original components (figure 1).

**FIGURE 1 - Acylaminoacids and their components**



Aminoacids and fatty acids are really important for skin and hair.

11% of the dry weight of the epidermis is comprised of free aminoacids, with the major portion present on the skin surface (stratum corneum). Furthermore while cystine and cysteine are absent from the epidermis (but present on the hair) all the remaining 19 aminoacids are present in the epidermis at concentration 200 times higher than plasma (1).

Some authors suggest the existence of micro channels for aminoacids permeation into human skin and the possibility to use aminoacids in order to maintain moisturization and prevent dry skin (4).

Actually we don't have to forget that NMF, that means the group of hydrosoluble substances present on the skin and responsible of its right hydration, contains about 40% of free aminoacids (table 1).

**TABLE 1 - NMF Composition**

NMF composition is the following (5, 6):

- 17 Free amino acids (including Glycine, Serine, Alanine, Asparagine, Ornithine, Citrulline, Proline and others) 40%
- PCA (mainly as Sodium salt) 12%
- Urea 7%
- Ammonia, uric acid, glucosamines, creatinine 1.5%
- Sodium 5%
- Calcium 1.5%
- Potassium 4%
- Magnesium 1.5%
- Phosphates 0.5%
- Chlorides 6%
- Lactates 12%
- Citrates, formiates 0.5%
- Undetermined fractions 8.5%

Free fatty acids in the horny layer are about 25% of the total lipids amount while in the lower layers they are only 5%. Free fatty acids are essential for the barrier effect of the skin (they keep skin supple, pliable and well moisturized) (3).

Fluhr et al. report that the generation of free fatty acids from phospholipids regulates the stratum corneum acidification and integrity (7). In this study, the results obtained by Fluhr and coworkers demonstrate the importance of phospholipids to free fatty acid processing for normal stratum corneum acidification. They underline the potentially important role of this pathway not only for barrier homeostasis but also for the dual function of stratum corneum integrity and cohesion. The application of palmitic, stearic or linoleic acid is able to normalize the stratum corneum pH and also functional abnormalities.

With acylaminoacid type surfactants we supply therefore the skin with its physiological components.

Major benefits and main applications of Acylglutamates can be so summarized:

***Major Benefits***

- moisturizing effect
- mild cleansing
- decrease SLES absorption
- aid in maintaining skin balance

***Main Applications***

- products for sensitive skin
- products for dry skin
- ethnic products
- baby care
- cold and traditional emulsions

## II. ACYLGLUTAMATES, SKIN AND HAIR

As said before the two components of acylglutamates, that means glutamic acid and free fatty acids, are very important for the health of skin and hair.

Glutamic acid is about 15% of keratins. Furthermore with its two carboxylic groups it helps the skin to maintain its natural acidity (1). In fact cutaneous acidic pH is also due to the presence of acidic proteins. However some pathological skin conditions can cause the decarboxylation of these lipoproteins, leading to the formation of amines and to a more alkaline and out of equilibrium pH value. The table shows the correlation between skin pH values and some skin disorders (8).

**TABLE 2 - pH and skin**

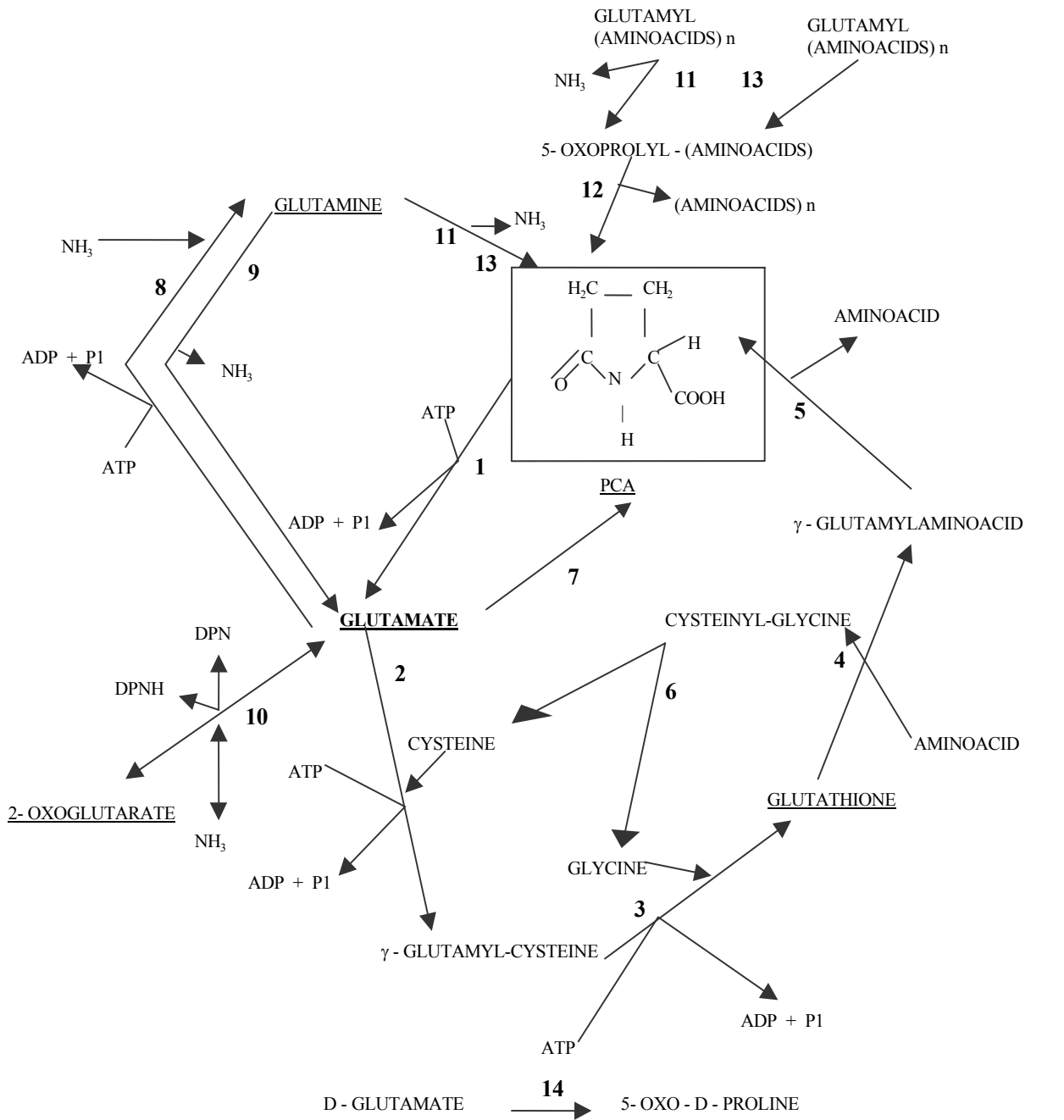
pH values	Skin disorders
5.0 - 5.2	healthy skin
5.2 - 5.5	seborrhea
5.5 - 6.0	mycotic affections
6.0 - 6.5	pyoderma
6.5 - 7.0	eczema
7.0 - 7.5	acne
7.5 - 8.0	pruritus (anal, genital)
8.0 - 9.0	intertrigo

A recent work (9) demonstrates that high pH values cause stratum corneum proteins swelling and increase lipid rigidity. In these conditions surfactants penetration is also enhanced.

Glutamic acid is also able to enter many metabolic cycles that take place in the epidermis; it is able for example to originate not only PCA but also proline and hydroxyproline (these two last aminoacids are very important for the synthesis of collagen and elastine) (1). Delapp and Dieckmann hypothesized the synthesis of PCA from glutamic acid contained in a slow turn over proteins pool (10).

Figure 2 shows the metabolic cycle of glutamic acid (6).

**FIGURE 2 - Glutamic acid cycle**



- |                                       |                                 |  |
|---------------------------------------|---------------------------------|--|
| 1) 5-Oxo-L-prolinase                  | 6) L-Cysteinylglycinase         | 11) L-Glutamine cyclotransferase   |
| 2) L-γ-Glutamyl-L-cysteine synthetase | 7) L-Glutamate cyclotransferase | 12) L-Pyrrolidone carboxylpeptidase (5-oxo-L-proline/carboxyl peptidase) |
| 3) Glutathione synthetase             | 8) L-Glutaminase                | 13) Non enzymatic  |
| 4) L-γ-Glutamyltranspeptidase         | 9) L-Glutaminase                | 14) D-Glutamate cyclotransferase   |
| 5) L-γ-Glutamylcyclotransferase       | 10) L-Glutamate dehydrogenase   |  |

Glutamic acid is also present in  $\epsilon$ -[ $\gamma$ -glutamyl]lysine bonds that covalently crosslink the two insoluble proteins of keratinocyte membrane, that means keratolinin and involucrin (1).

Glutamic acid is furthermore a biological precursor of ornithine. When skin is irradiated with UV there is an increase in the activity of the enzyme ornithine decarboxylase with development of toxic amines and decreasing of ornithine concentration. Glutamic acid can solve this problem (11).

Observations via SEM (Scanning Electron Microscopy) show that acylglutamates have a protecting and repairing effect on cuticle layer of hair (sodium laureth sulfate doesn't show the same effect) (12).

Acylglutamates belong to the so called "interrupted soaps" category molecules. This category of surfactants contains one or more mean polarity groups located between the hydrocarbon chain and the anionic polar group and exhibits higher skin tolerability than that of their homologous "uninterrupted" structures. This means that a group with intermediate polarity between the non-polar tail and the hydrophilic head acts as a buffer (or bridge), thus preventing strong bonds with proteins, as well as long-term irritating effects on the skin due to the surfactants residue. An amide group and carboxyl group are interposed in acylglutamates between the alkyl group and the carboxyl ion. The double carboxyl groups appear also in other surfactants (e.g. sulfosuccinates), which are well known for their mildness.

Acylglutamates are also able to decrease SLES absorption on skin.

From literature (13) it was proved that fast everybody has some amounts of Sodium Laureth Sulfate on the skin. This is because SLES is the most used primary surfactant.

Adding Sodium Cocoyl Glutamate to a standard formulation based on 10% of SLES was proved to lead to a significant reduction of SLES absorption (55% less with 25% of Sodium Cocoyl Glutamate in formulation). Sodium Cocoyl Glutamate itself is not absorbed on the skin.

### III. SELECTIVE DETERGENT POWER

As shown in paragraph I it is possible to speak of the “brick” and “cement” model in order to describe the epidermal barrier. The “cement” is made of intercellular lipids. These intercellular lipids are chemically very different from sebaceous gland secreted lipids, that means sebum. They fulfill a structural role in the preservation of the barrier function and integrity of stratum corneum and so while in lower layers lipids with a large water-binding capacity are present (glucosylceramides and/or phosphatidylcholine), in the upper layers we find molecules able to form liquid-crystalline structures. The high content of cholesterol and fatty acids allow this regular structure to be rigid and fluid in the meantime, fulfilling so barrier function.

If we have a look at the sebum composition (table 3) we can see a low cholesterol content and an high squalene content (8).

**TABLE 3 - Chemical composition of sebum**

Glycerides and free fatty acids	62.0%
Wax esters	25.0%
Squalene	12.0%
Cholesteryl esters	2.0%
Cholesterol	1.0%

If a surfactant is able to remove squalene and to leave cholesterol, we can say that it has a selective detergent power to sebum and that means that it's safe and mild to the skin (it doesn't affect structural lipids).

Furthermore we don't have to forget that babies haven't sebum (sebum is produced under hormones control); acylglutamates are therefore the choice surfactants for baby care.

#### IV. ACYLGLUTAMATES AS MOISTURIZING AGENTS

As seen before, Sodium Cocoyl Glutamate is able to reduce SLES skin absorption. Furthermore Sodium Cocoyl Glutamate was demonstrated to increase skin moisturization. In order to prove this a “short term moisturization test” with **Protelan AGL 95/C** was performed by Zschimmer & Schwarz (14).

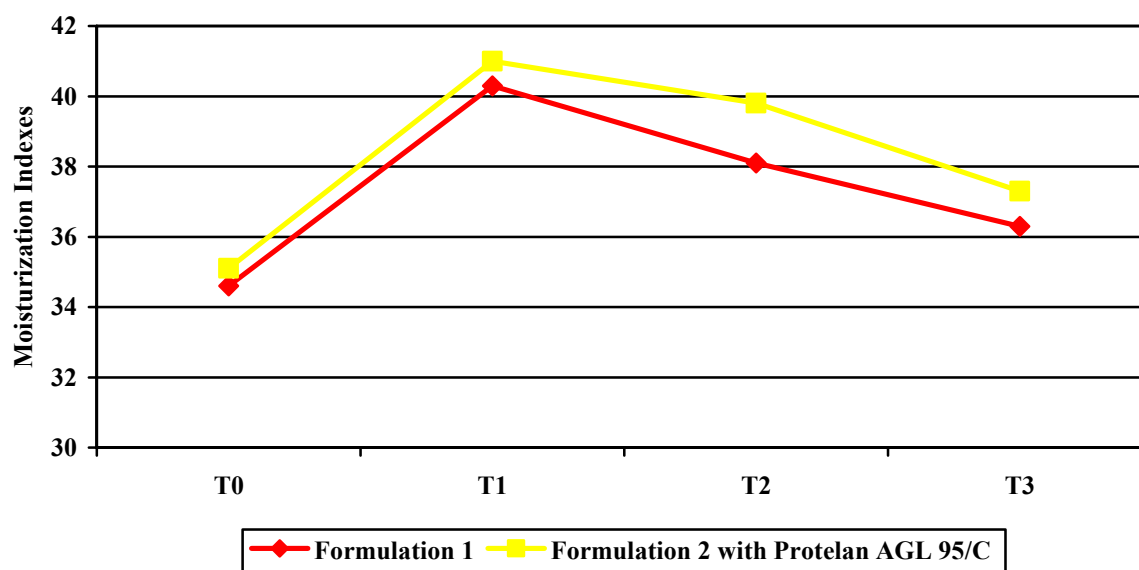
Two formulations were compared: one was a market formulation claimed to be a “24 hours moisturizer”, the second was the same formulation added with 5% of **Protelan AGL 95/C**. Dry matter and pH of both formulations have been brought to the same values.

40 subjects, both males and females, aged between 18 and 70 years, were used for the test. Twenty volunteers applied “formulation 1” on their forearm area selected for the test, the other group of twenty volunteers applied “formulation 2” (with **Protelan AGL 95/C**).

The moisturizing difference was evaluated by analysing the values taken with a corneometer before and after the product application. The readings were taken at T0 (basal value before the application) and 15 minutes [T1], 1 hour [T2] and 24 hours [T3] after product application.

The results are reported in figure 3.

FIGURE 3 - Short Term Moisturization Test



As it is possible to see both formulations have a significant moisturizing power, but the addition of **Protelan AGL 95/C** gives a more effective formulation (in a significant way).

## V. PROTELAN AGL 95 AND PROTELAN AGL 95/C AS EMULSIFIERS IN O/W EMULSIONS

**Protelan AGL 95** and **Protelan AGL 95/C** can be used as hydrophilic emulsifiers for the formulation of oil in water emulsions.

Their HLB value depends on pH value. Table 4 and Table 5 show this relationship.

**TABLE 4 - HLB values for Protelan AGL 95**

HLB values	pH
28.1	4.0
29.7	5.0
32.8	6.0
32.8	7.0
37.4	8.0
37.4	9.0
42.0	10.0

**TABLE 5 - HLB values for Protelan AGL 95/C**

HLB values	pH
32.8	4.0
34.3	5.0
35.9	6.0
35.9	7.0
40.5	8.0
40.5	9.0
45.1	10.0

As hydrophobic coemulsifier Cetareth-2 can be used. **Protelan AGL 95** and **Protelan AGL 95/C** are also able to form liquid crystalline (LC) gel network structures if mixed with low HLB non ionic emulsifier (for example cetaryl alcohol). The mechanism of the gel network formation can be described as follows. In a first step the hydrophilic surfactant (**Protelan AGL 95** or **AGL 95/C**) builds in the aqueous phase micelles that are present in a spherical form. In the presence of hydrophobic gel network formers such micelles grow and change their shape to disk types and with increasing concentrations of the co-surfactant to rod sphere micelles. During cooling to the melting point, the rodlike micelles consisting of the hydrophilic surfactant and the gel network forming co-surfactant turn into lamellar liquid crystalline structures and whilst further cooling into rigid liquid crystalline gel networks.

For each combination of gel network formers and “swelling agents” in a particular aqueous system (with particular electrolyte concentration, pH, choice of ingredients etc.), there is an optimal ratio of gellant to swellant to achieve maximum swelling. At such a maximum, the surfactant combination is referred to as “balanced”.

The use of acylglutamates is very simple. During the emulsion manufacturing they can be added to the water phase, the water phase is then heated to 65°C - 90°C (depending on the ingredients) and then the oil phase can be added even at room temperature if lipids are fluid. The standard manufacturing method can be also used.

**Protelan AGL 95** and **Protelan AGL 95/C** can be successfully used also with LEE (Low-Energy Emulsification) method where a concentrated emulsion is formed (with about 20-30% of the previous water) while the remainder water is added after during the cooling process.

**Protelan AGL 95** and **Protelan AGL 95/C** are also efficient wetting agents for powders and pigments.

**Protelan AGL 95** is furthermore the main ingredient of a completely vegetable and with outstanding performances self-emulsifying base for O/W emulsions (see **Protelan ENS** leaflet).

## VI. COSMETIC USES AND RECOMMENDATIONS OF EMPLOY

**Protelan AGL 95** and **Protelan AGL 95/C** can be used in a wide range of formulations. They are particularly suitable for sensitive skin and sensitive skin areas. Acylglutamates are the choice surfactant for baby care products.

Some examples of formulations are:

- Foam baths
- Shower gels
- Shampoos
- Hypoallergenic products
- Products for dry skin
- O/W emulsions
- Baby care products
- Ethnic products
- Products for elderly people

Very interesting is the use of **Protelan AGL 95** and **Protelan AGL 95/C** for ethnic products. In order to have a right approach to this problem is essential to understand the different characteristics of the skin and hair of people of ethnic origin.

Black skin has for example a tough outer layer of epidermis. This is prone to scarring, which can result in serious problems. Black skin also contains a greater number of sebaceous glands than white skin (40-60% more) (2).

Common skin conditions such as acne can lead to serious disfigurements for black skin. When formulating facial care products for black skin it is therefore especially important to select raw materials with very low comedogenicity in order to avoid irritation or the initiation of comedones or acne (2).

Ashy skin (xerosis) is a particular problem resulting from excessive drying of the skin. This can be caused by harsh detergents or environmental effects such as extreme cold spells or excessive dry heat. The condition manifests itself as dry white patches, commonly on elbows, knees and backs of hands. In areas where conditions are extremely dry, occlusive preparations inhibiting water loss are particularly valuable, although they would be entirely inappropriate for areas of high humidity (2). For all these conditions **Protelan AGL 95** and **Protelan AGL 95/C** are the right surfactants.

Also Caucasian and Afro-Caribbean hair is structured very differently. Caucasian hair is straight while Afro-Caribbean is tightly curled. In curly hair there is in fact a non-uniform distribution in that the disulphide bridges are more prevalent on one side of the hair fibre.

But the principal reason why specific products are required for treatment of Afro-Caribbean hair lies in the widespread use of chemical substances to restyle or straighten Afro hair.

In fact, these treatments rupture the bonds that link protein fibres and thus weaken the structure of the hair (2).

Consequently, formulations must be chosen with specific characteristics of mildness and ability to restore lustre, body and moisture content to chemically treated hair.

**Protelan AGL 95** and **Protelan AGL 95/C** are also very suitable for elderly people. For example elderly people's hands forearms and lower legs are particularly dry and with cold weather the stratum corneum quickly dries out (2).

A good moisturization is therefore fundamental.

**Protelan AGL 95** and **Protelan AGL 95/C** must be protected from cold. At low temperature and on prolonged storage they can become turbid. The material can be restored to its original appearance by indirect heating and stirring.