Chapter 2

Glycolic Acid

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The author has no financial interest in any of the products or equipment mentioned in this chapter.

Contents

2.1 History

In a study of more than 60 substances chosen for their possible antikeratinogenic properties, Van Scott and Yu [1] found that the most effective drug belongs to the group of alpha-hydroxy acids. A three times a day application of citric, glycolic, lactic, malic, pyruvic and glucuronic acid, for instance, gave excellent results in all forms of ichthyosis except epidermolytic hyperkeratosis. The substances were applied at 5% strength in a hydrophilic ointment, though the base was a matter of the patient's preference. Sustained remission was obtained as long as the treatment continued. The use of these agents has been extended to other hyperkeratotic conditions. Glycolic acid became available in the late 1980s as a peeling agent.

2.2 Chemical Background

Glycolic acid is an alpha-hydroxy acid, soluble in alcohol, derived from fruit and milk sugars. It can be produced with ethylene glycol-oxidizing microorganisms such as Pichia naganishii AKU 4267 and Rhodotorula sp. 3 Pr-126. Under optimized conditions, they form 105 and 110 g/l of glycolic acid (corrected molar conversion yields 88.0 and 92.2%) during a 120-h reaction, respectively [2].

2.3 Properties

It has been shown that glycolic acid has a keratolytic, germinative layer and a fibroblast stimulating action.

Reported studies have shown its anti-inflammatory effects and anti-oxidant action. It acts by thinning the stratum corneum, promoting epidermolysis, dispersing basal layer melanin and epidermal and dermal hyaluronic acid and collagen gene expression that increases through an elevated secretion of IL-6 [3].

2.4 Formulations

The absorption of glycolic acid in human skin is pH-, strength- and time-dependent. Seventy percent glycolic acid solutions are commonly

used as superficial chemical peeling agents, the pH of these solutions ranges from 0.08 to 2.75. Peeling solutions with a pH below 2 have demonstrated the potential to induce crusting and necrosis, which has not been seen with the partially neutralized solutions with a pH above 2 [4]. The higher concentration acid (70%) created more tissue damage than the lower concentration (50%) compared to solutions with free acid. An increase of transmembrane permeability coefficient is observed with a decrease in pH, providing a possible explanation for the effectiveness of glycolic acid in skin treatment.

2.5 Indications

Glycolic acid has been recognized as an important adjunctive therapy in a variety of conditions including photodamage, acne, rosacea, striae albae pseudofolliculitis barbae, hyperpigmentation disorders, actinic keratoses, fine wrinkles, lentigines, melasma and seborrheic keratoses [5]. Moreover, it can reduce UV-induced skin tumor development and it has been proposed as a therapeutic modality against skin exfoliative conditions such as ichthyosis, xeroderma and psoriasis. In post-menopausal women a cream containing 0.01% estradiol and 15% glycolic acid, applied to one side of the face for 6 months, induces a significant improvement in reversing markers (rete peg pattern, epidermal thickness) of skin aging [6].

Glycolic acid chemical peels are an effective treatment for all types of acne, inducing rapid improvement and restoration of normal-looking skin. In these patients glycolic acid is more widely used than Jessner's solution, considering the equal treatment effect but a reduced exfoliation in glycolic acid [7]. Although the treatment of atrophic acne scars is difficult and generally unsatisfactory, many clinical studies have been performed to investigate the efficacy of glycolic acid in the treatment of acne vulgaris.

It is now widely used to treat many defects of the epidermis and papillary dermis in a variety of strengths, ranging from 20 to 70%, depending on the condition being treated [8].

2.6 Contraindications

Glycolic acid peels are contraindicated in contact dermatitis, pregnancy and in patients with glycolate hypersensitivity. Moreover, they can increase skin sensitivity to ultraviolet light.

2.7 Peeling Preparation

Patients with photodamage can apply a lotion containing 25% glycolic acid for 6 months. In such cases an increase in total skin thickness of approximately 25% was reported, accompanied by an increased thickness of viable epidermis and dermis, an increased content of acid mucopolysaccharides, a greater collagen density and an improved quality of the elastic fibers. This could be defined as self-treatment.

However, a better efficiency in peeling can be achieved with a concentration of 50–70% of glycolic acid and, for maximum benefit, glycolic acid peels are combined with retinoids and other antioxidants. Some studies have evaluated the efficacy of a cream containing 4% hydroquinone and 2% glycolic acid used alone or with salicylic acid in reversing actinic damage on the neck and upper chest for 12 weeks; salicylic acid peelings are performed every 3 weeks. This treatment induces a 33–71% improvement in cases of photodamage (Figs. 2.1a, b and 2.2a, b), hyperpigmentation, texture problems, fine lines, dryness, tone and clarity [9].

Other studies have demonstrated that the application of 50% glycolic acid peels mildly improves photoaging of the skin. Generally, for a light peeling, glycolic acid (50%) was applied topically for 5 min to one side of the face, forearms, and hands, once weekly for 4 weeks. The improvement observed was significant and included decrease in rough texture and fine wrinkling, fewer solar keratoses and a slight lightening of solar lentigines. Histology showed thinning of the stratum corneum, granular layer enhancement, and epidermal thickening. Longer treatment intervals may result in collagen deposition as suggested by the measured increase in mRNA.

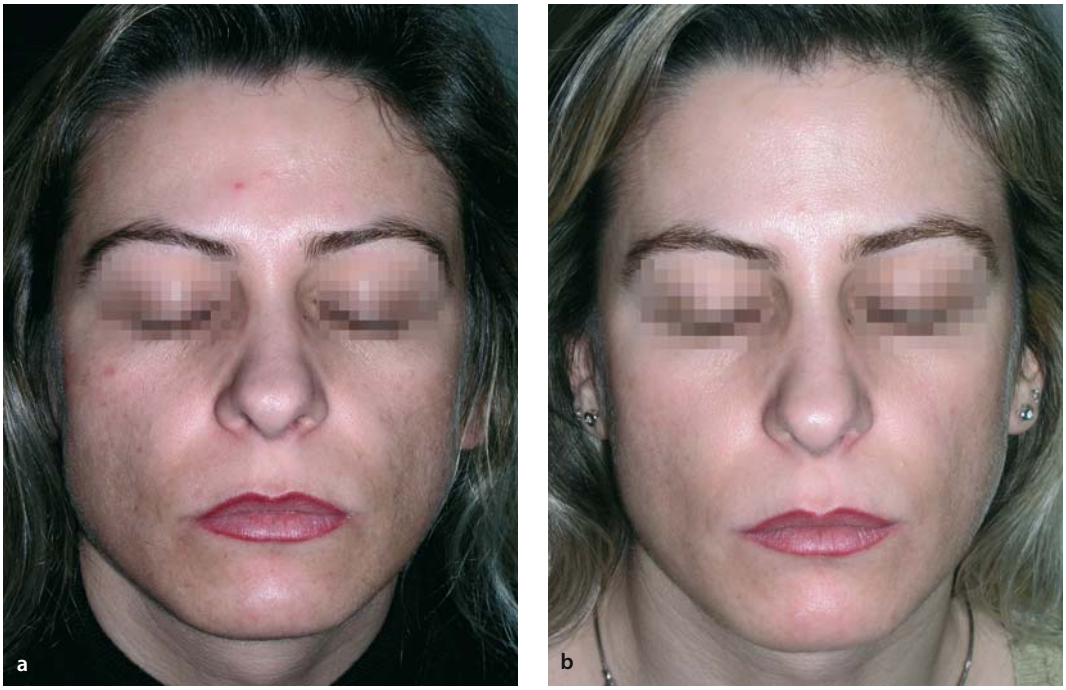

Fig. 2.1a, b. Improvement of photodamage after chemical peeling

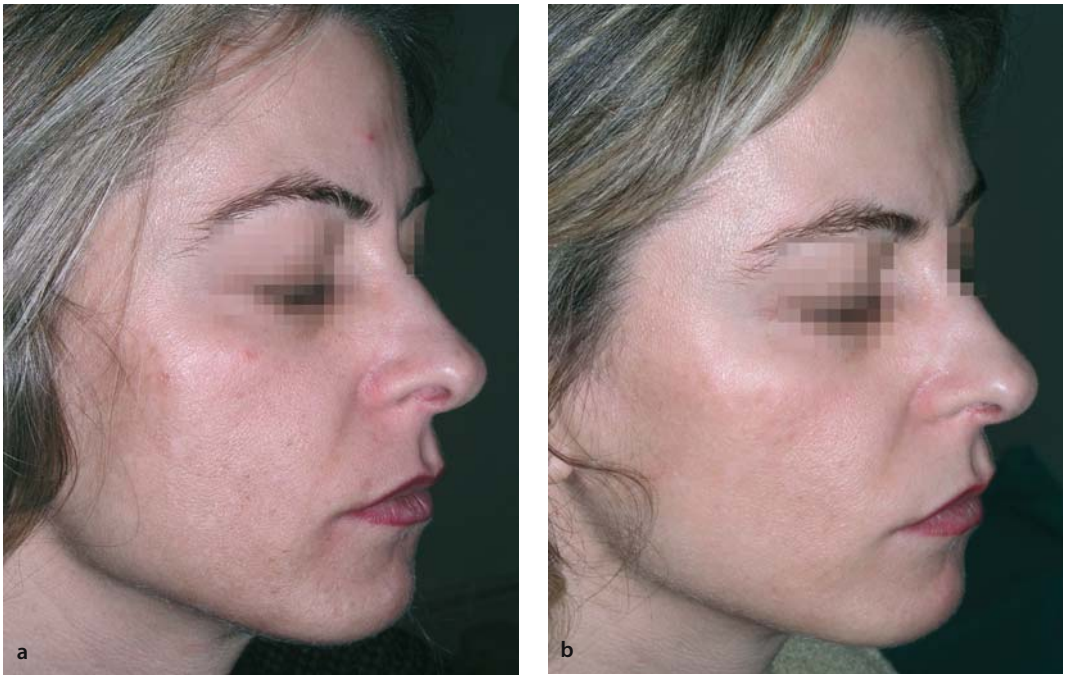

Fig. 2.2a, b. Lateral view of the same patient before and after peeling

2.8 Peeling Technique

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Before applying glycolic acid the skin is cleaned with alcohol to reduce the acid neutralized by oily skin. Glycolic acid is applied in any cosmetic unit order, rapidly covering the entire face within about 20 s with a large cotton applicator. A starting application time for weekly or monthly applications with 50 or 70% unbuffered glycolic acid is generally in the range of 3 min, and the time is increased with subsequent peels. Neutralizers with sodium bicarbonate marketed to the physician have no advantage over water rinsing as long as all acid is removed thoroughly from all rhytidis and cosmetic units.

Glycolic acid applied simultaneously with TCA represents another technique for a medium-depth peel. Several weeks prior to a peel the skin may be prepared with topical tretinoin or glycolic acid, and immediately prior to the peel the skin may be degreased with a variety of agents. Some studies demonstrated that glycolic acid-trichloroacetic acid peels, called combination medium-depth peeling, are usually performed as a single procedure to remove actinic keratoses, mild rhytidis, or pigmentary dyschromias or to flatten depressed scars. These peelings can be repeated approximately every 6 or 12 months based on the amount of actinic damage still remaining or recurring after the peel or for continued scar effacement. The classic peel for this depth category was the 50% TCA peel.

Since TCA in higher concentrations tends to produce increased scarring and hypopigmentation, 70% glycolic acid solution was applied to the entire face of patients and diluted with water after 2 min. This was followed by the sequential application of EMLA cream (lidocaine 2.5% and prilocaine 2.5%) or ELA-Max cream (lidocaine 4%) to selected areas on the face for 30 min without occlusion. These agents were then removed and 35% TCA was applied to the entire face [10].

Patients with melasma (Fig. 2.3) applied topical sunscreens (sun protection factor 15) and 10% glycolic acid lotion at night for 2 weeks. They were then treated with 50% glycolic acid facial peels once a month for 3 consecutive months. At regular intervals and at the end of the follow-up period (3 months) after the last peel, the degree of improvement in pigmentation was assessed by measuring MASI (Melasma Area and Severity Index) [11].

In patients with acne (Fig. 2.4), the chemical peels were performed with a 70% glycolic acid solution, for 2 to8 min. The number and frequency of the applications depended on the intensity of the clinical response. The most rapid improvement was observed in comedonic acne, in the papulo-pustular forms. An average of six applications were necessary (Fig. 2.5a, b).

Although nodular-cystic forms required eight to ten applications, a significant improvement of the coexisting post-acne superficial scarring was noted. The procedure was well tolerated and patient compliance was excellent [12]. In the treatment of atrophic acne scars (Fig. 2.6),

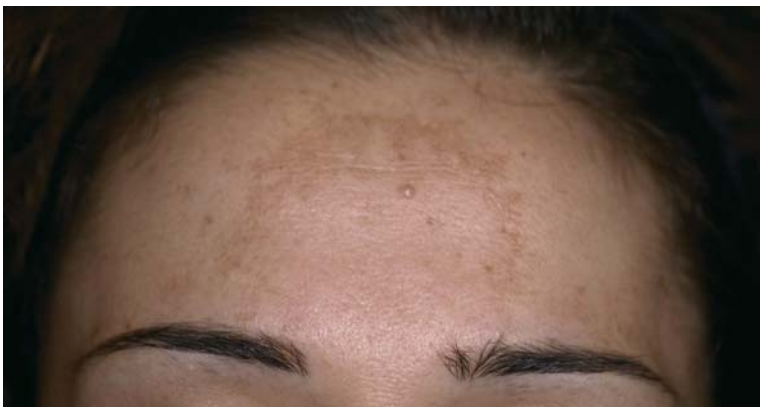


Fig. 2.3.
Melasma of the forehead

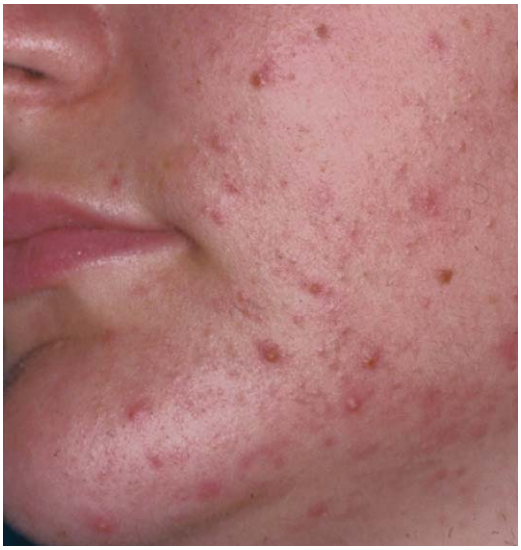


Fig. 2.4. Papulo-pustular acne

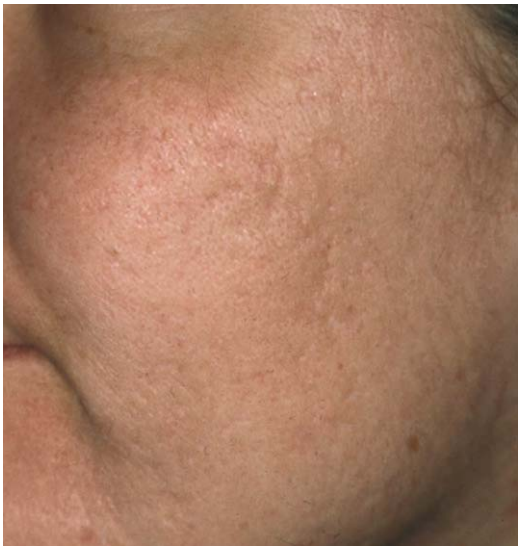
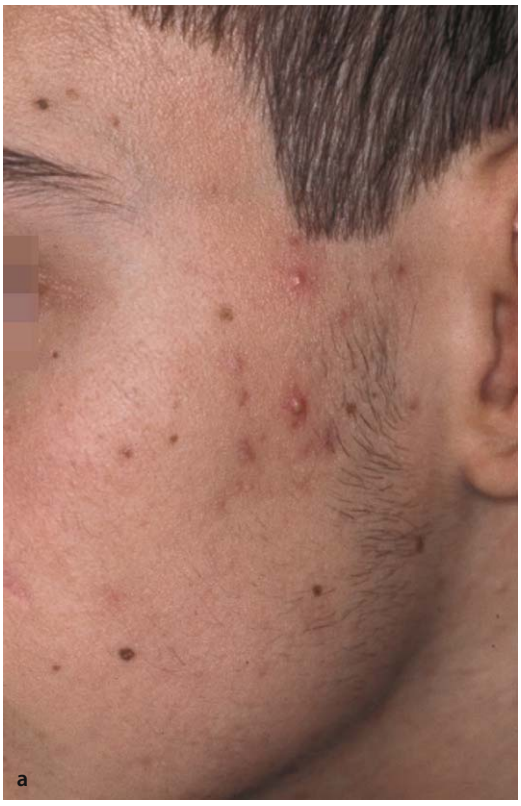


Fig. 2.6. Atrophic acne scars



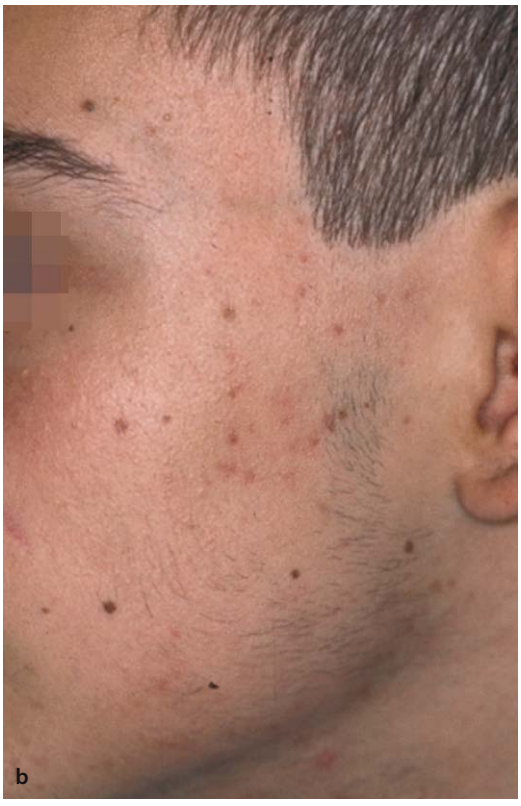
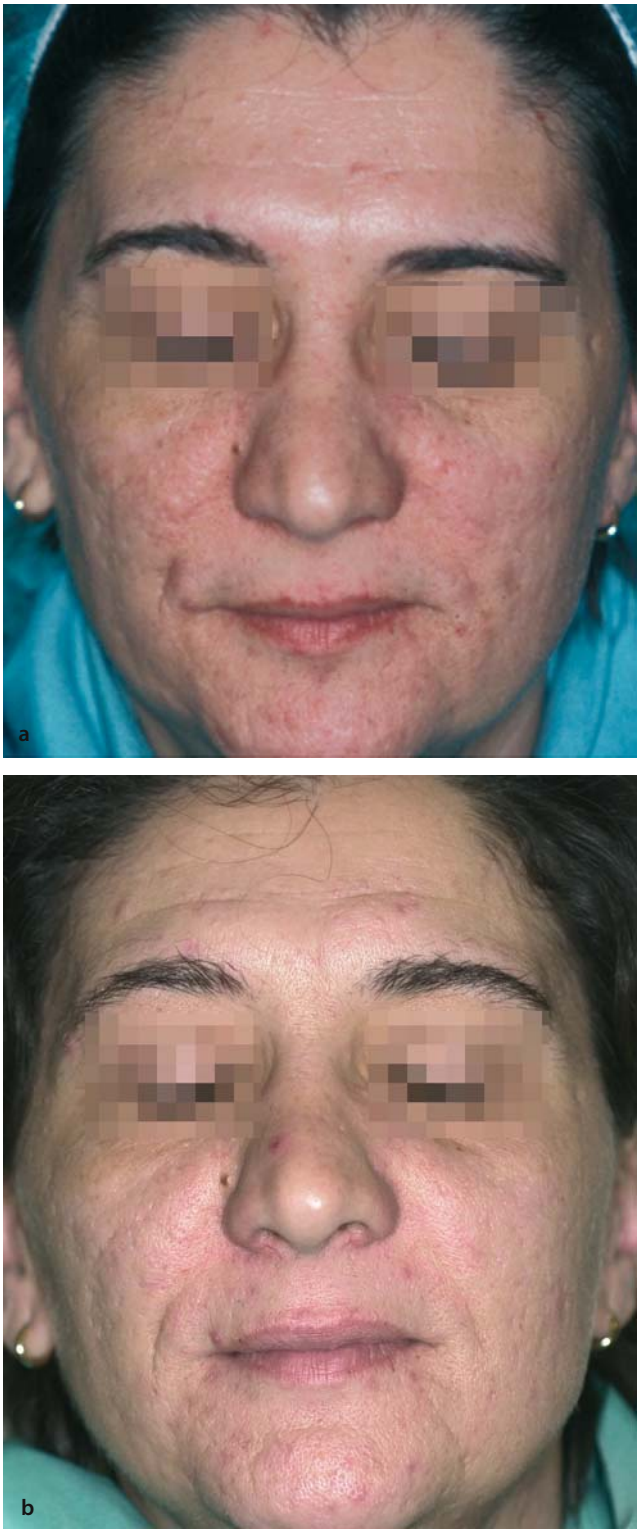


Fig. 2.5a, b. Papulo-pustular acne before and after peeling

Fig. 2.7a, b. Acne scars before and after 70% glycolic acid peeling



repetitive glycolic acid peels (at least six times) at 70% concentration are necessary to obtain evident improvement. Long-term daily use of low-strength products may also have some useful effects on scars and may be recommended for patients who cannot tolerate the peeling procedure [13] (Fig. 2.7a, b).

Patients of varying skin types (I–V) having striae distensae alba on the abdomen or thighs can apply topical 20% glycolic acid daily to the entire treatment area. In addition, these patients apply 10% L-ascorbic acid, 2% zinc sulfate, and 0.5% tyrosine to half of the treatment area and 0.05% tretinoin emollient cream to the other half of the treatment area. The creams are applied on a daily basis for 12 weeks. Improvement is evaluated at 4 and 12 weeks with increased elastin content within the reticular and papillary dermis [14].

Pseudofolliculitis barbae is a foreign-body inflammatory reaction surrounding ingrown facial hair, which results from shaving. Topical application of glycolic acid lotion is an effective therapy and allows the patient to resume a daily shaving regimen [15].

In patients with scalp psoriasis a combination of a 10% glycolic acid scalp lotion is used as well as a 0.1% betamethasone scalp application, applied twice daily without any bandage for a period of 8 weeks [16].

2.9 Post-peeling Care and Complications

Following the peel the skin is carefully observed for any complications such as hyperpigmentation and infection. Results are maintained with serial peels and by using at-home tretinoin or glycolic acid, as well as by sun avoidance.

2.10 Disadvantages

Through the patient's history and physical examination, the physicians will identify any specific factor such as medications, prior procedures and medical conditions that can affect the outcome of the peel [17]. Complications of glycolic acid peel like hyperpigmentation and infection are rare. Chemical peel with glycolic acid may cause sensible irritation symptoms, characterized by stinging, burning and itching. A substance capable of counteracting sensory irritation is strontium nitrate at 20 % concentration, which applied topically with 70% glycolic acid, potently suppresses the sensation of chemically induced irritation [18].

Moreover, some studies have demonstrated that glycolic acid could cause an increase in the level of skin damage in a dose- and time-dependent manner. Lower doses (1 and 3 mg/cm^2) of glycolic acid caused erythema and eschar at most, whereas higher doses (5 and 7 mg/cm^2) of glycolic acid caused redness, edema and necrotic ulceration.

Glycolic acid also increased the thickness of the epidermal layer, reduced the organization of the stratum corneum and eventually destroyed some parts of the epidermal layer at 7 mg/cm^2. UVB caused redness and edema and also reduced the integrity of the stratum corneum. Glycolic acid enhances UVB-induced skin damage without accompanying PGE (2) production or COX-2 protein expression. Therefore, caution should be exercised by those using glycolic acid chronically or in excessive amounts. Moreover, people with photosensitive skins and those particularly exposed to the sun should be particularly careful. However, this photosensitivity could be reversed within a week after terminating treatments [19].

Laboratory investigations have rarely shown a complex I deficiency in the mitochondrial oxidative phosphorylation of patients who had recurrent episodes characterized by nausea, vomiting, and signs of dehydration necessitating admission to the hospital. In these patients glycolic acid was detected in blood and they were diagnosed as having ethylene glycol intoxication [3].

2.11 Side Effects

Side effects, such as temporary hyperpigmentation or irritation, are not very significant.

2.12 Results

Finally, glycolic acid is a member of the alpha-hydroxy acid family, which provides an important adjunctive therapy in a variety of skin disorders. It is widely used in chemical peels in a variety of concentrations, ranging from 20 to 70%. People of almost any skin type and color are candidates and almost any area of the body can be peeled.

Glycolic acid can be applied simultaneously with TCA, which represents another technique for a medium-depth peel. Glycolic acid is also used in creams for self-treatment. Since complications such as hyperpigmentation, infection, irritation, and photosensitivity are very rare, it is well tolerated.

2.13 Informed Consent

Glycolic acid peeling is a medical procedure that requires the informed consent of the patient. The medical doctor must obtain from the patient a well-standardized formal consent that shows that all information about the medical procedure performed was explained to the patient. We include below the formal consent form submitted to the patient before the glycolic acid peeling procedure.

I, _____, after carefully reading the information regarding the glycolic acid peeling prodedure, give my informed consent to undergo glycolic acid peeling treatment.

I have been well informed about side effects that the procedure could cause.

I have been well informed of temporary effects of the therapy.

I confirm that I have informed the medical doctor about all actual pathologies or pathologies that I have had.

I confirm that I have informed the medical doctor about pharmacological therapies that I am currently receiving or have received in the past.

I confirm that I want to perform the treatment of my own free will without any physical or moral conditioning and I confirm that I have the right to interrupt the therapy such as I want without the necessity of justifying my decision.

Surname and name

Date of birth

Place of birth

Address

Town

Tel

Signature of the patient

Date

I, medical doctor, _____, confirm that I have explained with accuracy the type, aim and possible risks of the medical procedure to be performed on the patient indicated, who has given consent to begin the treatment.

Surname and name of the medical doctor

Signature of the medical doctor

Date

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