Chapter 1
Keratolytic peels

The first peeling agents for medical purposes were keratolytic substances. Phenol, trichloroacetic acid, salicylic acid, and resorcinol have been used to treat scars and pigment spots since the 1880s. The term "keratolytic" was coined to describe the action of these compounds, which means "dissolver of horny scales" (from the Greek κέρατο — horn).

This name was given because when keratolytic substances were applied to the skin, a whitish plaque appeared on the surface, which was then easily washed off. Most plaque is built up of modified corneocytes filled with keratin. But keratin is not the only target for keratolytic agents, so in addition to their exfoliating effect, they are also characterized by other effects.

1.1. Features of keratolytic peels

1.1.1. Mechanism of action

Keratolytic agents react with proteins to **break the disulfide bonds** between the sulfur atoms of the amino acid cysteine (**Fig. II-1-1**). A covalent bond formed between two cysteines on one amino acid chain is called intramolecular while that formed on different chains is denoted as intermolecular.

With the help of disulfide bonds, a protein (or a protein complex, if it is composed of several chains) maintains a particular 3D configuration. Such a protein is called **native**, and only in native form it can perform the functions assigned to it, whether structural, enzymatic, or otherwise. As a result of breaking the stabilizing bonds, the protein unfolds and turns into an amino acid chain — a **denatured** protein that is no longer functional.

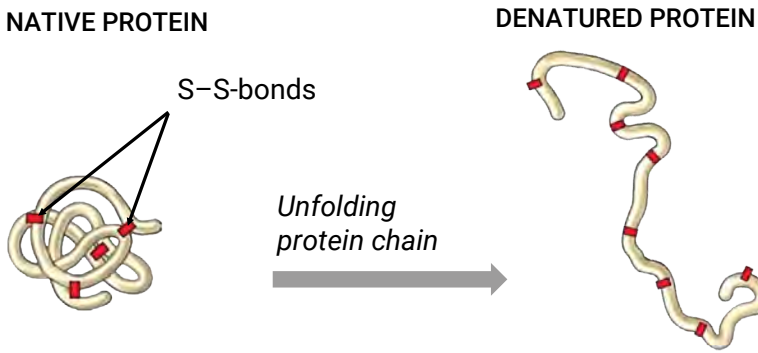

Figure II-1-1. Mechanism of keratolytic action: breaking of stabilizing disulfide bonds (–S–S–) in a protein molecule or protein complex

1.1.2. Skin targets for keratolytic agents

Keratolytics interact with ALL proteins stabilized by disulfide bonds, i.e., their action is not selective and is not limited to keratin. In addition to keratin, other proteins in the *stratum corneum* and epidermis can also be denatured when encountering a keratolytic agent, affecting the clinical result.

Skin surface

All keratolytics are antiseptics. They chemically modify **the proteins of the shells of microorganisms** (e.g., bacteria, fungi, and even viruses) in the area of application. If the wall damage is extensive, the microorganism dies.

The *stratum corneum* contains the following keratolytic targets (**Fig. II-1-2**):

- **Corneocyte proteins** — keratin (inside the corneocytes) and the cornified envelope proteins*
- **Corneodesmosomes** — protein bridges that bind corneocytes together and maintain the integrity of the *stratum corneum*

* The corneocytes are surrounded by a proteinaceous structure called the cornified envelope. This structure consists of a layer of highly cross-linked insoluble proteins covalently bound to a layer of lipids.

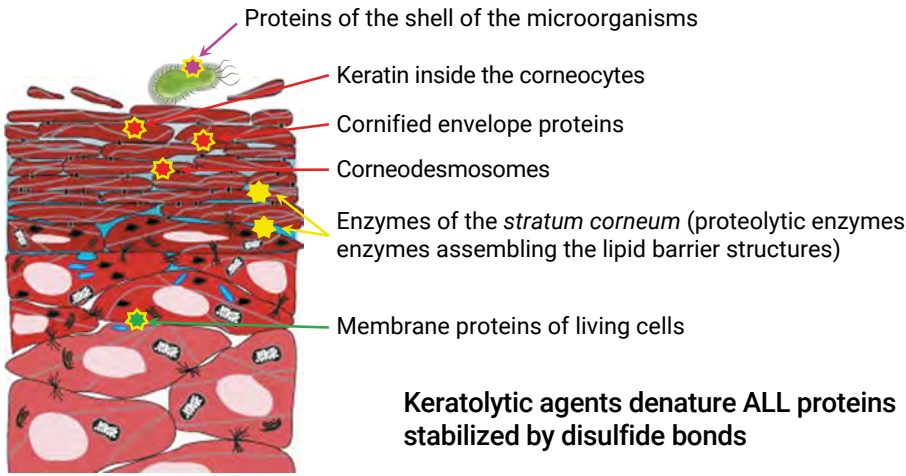

Figure II-1-2. Targets for keratolytic agents

- **Enzymes** — proteolytic enzymes (they "cut" the corneodesmosomes and are responsible for desquamation) and enzymes assembling the lipid barrier between the corneocytes

Living layers

What happens if the substance passes through the *stratum corneum* and ends up in the living cells' territory? The same process occurs — the keratolytic agent reacts chemically with the proteins, damaging their structure. The greatest danger to living cells is damage to **the cell membrane proteins that form the pores** — if they are denatured, the membrane ceases to filter the flow of substances entering and leaving the cell, and the cell quickly dies. All living cells — not only keratinocytes but also melanocytes, immunocytes, and skin receptors — are defenseless against keratolytic agents.

A person feels **pain** when a keratolytic agent enters the epidermis, which is attributed to the chemical damage to the membrane proteins of the skin receptors. To get rid of the damaging substance, living cells release various mediators, including vasodilators, to accelerate blood flow to the area and ensure the dissolution and excretion of the keratolytic agent. Therefore, erythema and edema indicate that the keratolytic agent has passed through the barrier and has reached the living cells.

Keratolytics are not selective — all cells in their path are attacked. This explains the inherent cytotoxicity of all keratolytic substances. Therefore, they should not be allowed to penetrate the *stratum corneum* without a strong reason.

1.1.3. Features of keratolytic peeling

Keratolytic peels have their peculiarities, both clinical and practical. All keratolytics are characterized by the appearance of the so-called **frost** on the skin during the procedure — a whitish plaque composed of denatured skin proteins.

Frost is an indication that the keratolytic agent has begun to work. In addition, it indicates the degree of skin damage (**Fig. II-1-3**). Thus, for TCA peeling, frost is used to control the reaction depth and determine when to stop the procedure. For phenol, dense frost appears quickly after the application.

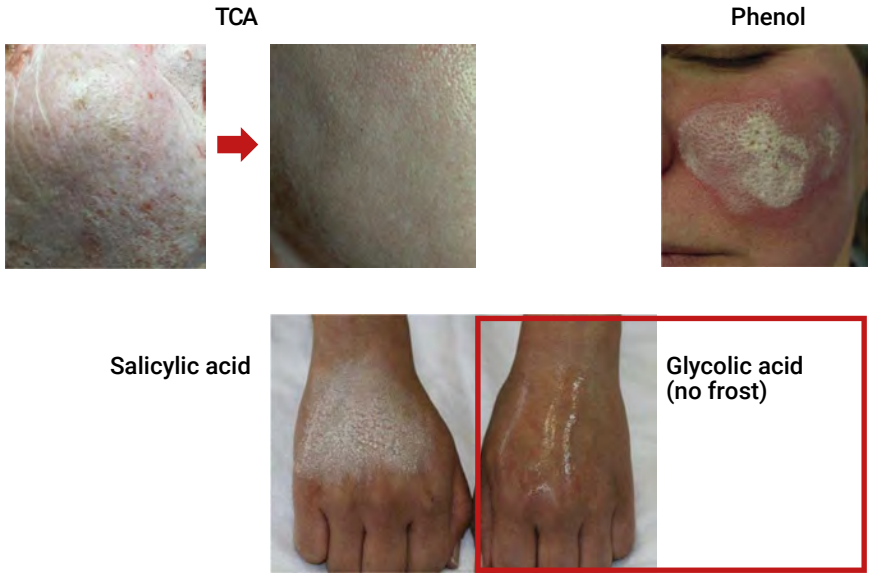

Figure II-1-3. Keratolytic peeling feature: whitish plaque on the skin (frost)

It is surrounded by erythema which is a sign of severe skin irritation. There is no redness during conventional superficial salicylic peeling, only a light plaque (unlike the frost with TCA and phenol, salicylic frost is sometimes called pseudo-frost, but it has the same origin and is composed of denatured proteins). There may be mild redness with superficial/medium-depth frost. In comparison, when treating with other peeling agents (AHAs, enzymes, retinol), there is no frost because there is no protein denaturation. These agents have different mechanisms of action, as we will explain in the corresponding sections.

The degree and speed of skin damage depend on:

1. Concentration of the keratolytic in the preparation — the higher it is, the more extensive the damage
2. Exposure duration — the longer it is, the more extensive the damage
3. Condition of the *stratum corneum* — the thinner it is, the greater the chances for substances to pass through it and get to the living layers

Depending on these parameters, the damage can be superficial (at the level of the *stratum corneum*) or deeper, affecting the living layers of the epidermis. **Unlike acid peels, keratolytic peels do not need to be neutralized.** The keratolytic mechanism is based on a chemical reaction with proteins independent of the pH value. To stop the keratolytic action and remove it from the skin, it is necessary to wash the skin thoroughly with water or a special solution that removes poorly water-soluble substances, which include keratolytics.

Keratolytic substances vary in ability to penetrate the *stratum corneum* and toxicity levels. Phenol and TCA are the most hazardous, and despite being prohibited in the cosmetics industry, they can still be found on the gray market.

We hope that the information presented in our book will serve as a warning to those who continue to use phenol and TCA in their practice and make them think about whether it is worth risking the health of their patients for no good reason (Wambier C.G. et al., 2019).