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TEMPERATURE-ACTIVATED ENZYMATIC EXFOLIATION AS A NON-IRRITANT RESURFACING ALTERNATIVE: BIOCHEMICAL RATIONALE AND IN-VIVO SKIN RESPONSE

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Abstract. *The article is devoted to the study of temperature-activated enzymatic peeling as a gentle, non-aggressive alternative to traditional chemical methods of skin renewal. The purpose of the article is to show the biochemical features of peeling and review the clinical results of their use. During the scientific study, general scientific methods of cognition were used: analysis, synthesis, modeling, observation, comparison, experiment, generalization. The results of the study show that enzymatic exfoliation is based on a targeted effect on the protein components of the stratum corneum - in particular keratin and corneodesmosomes – without damaging viable cells. The use of papain, bromelain and keratinase enzymes provides selective hydrolysis of intercellular bonds in the surface layer of the skin, contributing to the delicate removal of dead cells. Unlike acid peels, enzymatic formulas do not provoke coagulation damage to proteins and have a lower risk of irritation, which is confirmed by the clinical absence of pathological inflammation. It has been proven that temperature-activated enzymes demonstrate high efficiency under conditions of maintaining the physicochemical optimum – in particular, the skin surface temperature (32–34°C) and pH 4.7–5.9. Due to this, enzyme activation is achieved without loss of stability, which ensures controlled micropeeling. In clinical practice, temperature-activated enzyme peels have proven high efficiency and tolerability: most participants noted an improvement in skin texture, tone, and barrier integrity without the development of undesirable reactions. In particular, in cases of dry or oily skin, an improvement in elasticity, a decrease in the appearance of comedones, and an even microrelief were observed. The presence of short-term erythema without an inflammatory response additionally indicates the safety of this technology. The practical significance of the study lies in the introduction of a non-aggressive, effective approach to skin exfoliation, which allows preserving its barrier functions and reducing the risk of irritation during regular care.*

Keywords: *enzymatic peeling, enzymes, SAE complex, exfoliation, temperature.*

Introduction The global exfoliation market is driven primarily by the demand for effective and safe removal of the stratum corneum, which is directly reflected in the statistical indicators of the use of peeling products. In 2023, more than 58% of users of skin care cosmetics in the world regularly used exfoliating products at least twice a week, and in the US, 71 million women aged 18–54 years purchased scrubs or peels in the last 12 months [5]. At a structural level, the market is focused on those formats that provide a quick noticeable renewal of the skin surface, most often facial skin. Exfoliating scrubs occupy about 31% of the market in 2023, and 44% of units sold were natural or organic formulations, which emphasizes the global transition to enzymatic and plant-based peels and the rejection of polymer microbeads.

The overall economic dynamics clearly show the constant growth of the exfoliation industry: if in 2024 its financial assessment reached about 1.98 billion dollars, then in 2025 at least 2.09 billion dollars are expected. The market forecast until 2034 is over 3.31 billion dollars. The average annual growth rate is about 5.2%, which also corresponds to short-term forecasts: during 2024-2029 the market should additionally increase by almost 709 million dollars at a rate of 4.5% per year.

In this combination of behavioral, technological and financial indicators, it is clearly visible that peeling products, regardless of whether they are based on acids or enzymes, have become a systemic element of skin care, and their market demonstrates trends towards a combined combination of technologies in order to obtain greater efficiency and reduce the risks of the procedure.

Literature Review The issue of temperature-activated enzymatic peeling as a non-aggressive alternative for skin renewal is sufficiently studied in the world scientific literature. The analysis of statistical significance for economics is reflected in the source [4]. The biochemical mechanisms of action of enzymes used in enzymatic peeling are analyzed in detail in the works of K. Białkowski, P. Nowak, M. Sokolowska [1], T.C. Trevisol et al. [7], V. Venetikidou et al. [8], H. Zhou et al. [10]. They highlight the activity of enzymes such as bromelain, papain and ficin, describing their substrate specificity and the effect of temperature on activity.

The clinical efficacy and safety of mild enzymatic peelings is highlighted in the study of J. Namkoong et al. [5], which combines laboratory testing with an open clinical trial on patients with sensitive and normal skin. The work of S.N. has a similar applied focus. Dogiparthi et al. [2,3], which analyzes the effectiveness of organic peels, including enzymatic agents.

The purpose of the article is to show the biochemical features of peels and review the clinical results of their use.

Research Results

Enzymatic peeling is a process that relies on the natural biochemical mechanisms of physiological desquamation of the stratum corneum. In the stratum corneum, structural integrity is provided by protein complexes – primarily keratin and

corneodesmosomes, which hold corneocytes in a tightly organized matrix [8]. The strength of skin cells is determined by keratin, and the strength of the connecting elements of cells – corneodesmosomes, both of which are important elements that form healthy skin. The enzyme-based peeling procedure is based on the degradation of protein structures that form the stratum corneum of the skin. These enzymes do not affect the cells or the connecting elements of cells, but the corneocytes (cornified skin). As a result, extracellular formations exfoliate more easily, which allows the skin to renew itself faster. This phenomenon is modeled by the hydrolysis of casein, which is a suitable protein target for assessing the activity of cysteine proteases. Sources of such powerful acidic substances that can break down corneocytes are pineapple (bromelain), papaya (papain) and keratinase enzymes. They are able to break down numerous peptide bonds, which reflects their potential to destroy intercellular protein components in the surface layers of the epidermis [1]. Let us consider the features of each substance in Table 1.

So, the biochemical specificity of such peeling is the selective effect on protein substrates localized in the outer, already non-cellular-active layer of the skin, avoiding damage to viable cell structures [7].

Different classes of proteases: papain, bromelain, keratinases and microbial enzymes, demonstrate different properties that allow them to be used in cosmetic procedures. In general, they contribute to the uniform separation of corneocytes, improve the optical and structural parameters of the skin, without causing coagulation damage to proteins or excessive irritant response, characteristic of acidic products. The skin itself retains its barrier integrity, while at the same time acquiring greater smoothness and uniformity of the surface [7].

In practice, other chemical (non-natural) products are also often used, but natural sources show better efficiency. For example, pineapple extract is characterized by high proteolytic activity, while papaya shows approximately 120 times lower activity, which indicates different biochemical efficiency of natural proteases. Against this background, most of the tested cosmetic products do not show a noticeable ability to break down casein, despite their labeling as “enzymatic” [1].

Table 1 – Use of different reagents for peeling: advantages, features, concentrations

Parameter	Papain	Bromelain	Keratinase
Key action	hydrolyzes keratin and proteins of surface skin cells	gentle exfoliation without irritation	breaks down compacted follicular plugs, comedolytic effect
Optimal areas of use	face, body	sensitive skin, post-procedure conditions	scalp, oily/acne-prone skin
Product formats	serums, masks, gentle scrubs	light creams, gels, leave-on	serums, peels, cleansing products
Recommended facial concentrations	0.5–0.8%	0.3–0.7%	0.2–0.5%
Recommended body concentrations	0.5–1.0%	0.5–1.0%	0.4–0.6%
Use on lips	0.1–0.3%	0.1–0.2%	not used
Use on scalp	0.3–0.5%	0.2–0.4%	0.5–0.8%
Compatibility with sensitive skin	moderate	best	limited, requires exposure time control
Risks of overuse	transient irritation	minimal	disruption of protein matrix, increased TEWL
Advantages	fast results, versatility	high tolerance, low inflammatory response	significant reduction in comedones and sebum production
Dosage format	higher concentrations — for rinse-off	lower concentrations — for leave-on	controlled exposure, more often rinse-off
Most common user profile	normal/combination skin	atopic, reactive, post-procedure	seborrheic, acne-prone, with follicular hyperkeratosis

Note: systematized by the author based on the source [3]

The catalytic mechanism (e.g., temperature) of such enzymes is based on the presence in the active center of a reactive sulfhydryl residue of cysteine, which, in combination with histidine and associated amino acids, provides a nucleophilic attack on peptide bonds of proteins. The temperature range providing the optimum of enzymatic activity is located within the physiological thermal effect, while an increase in temperature above a stable threshold causes protein denaturation and loss of catalysis. That is why temperature-activated formulas that enhance activity without transitioning to destructive modes have special potential [8].

The effectiveness of this process is inextricably linked to the observance of optimal physicochemical parameters of enzyme functioning. Deviation from these conditions leads to partial or complete loss of the active state, which reduces or eliminates the exfoliating effect. For example, the activity of papain in solution can decrease by more than 90% within a month at room temperature, and bromelain is subject to immediate inhibition in certain gel matrices. This means that enzymes can lose their biochemical activity long before the consumer uses the product, which nullifies the mechanism of enzymatic peeling itself [1]. Therefore, the development of stable enzyme systems for application to the skin requires careful protection against denaturing environmental factors [7].

Thus, enzymatic peeling is a naturally integrated biochemical technology that combines:

- structural validity of the action – at the level of protein components of the stratum corneum;
- catalytic selectivity – aimed specifically at “dead” cells;
- physiological compliance of conditions – optimal pH and temperature range;
- the need for enzyme stabilization – to maintain the active state throughout the product's life cycle.

In clinical skin reactions, thermal-enzymatic peeling demonstrates reproducible statistical patterns, which are confirmed by the results of the use of enzymatic and organic exfoliants in in vivo studies. In most cases, the superficial skin response is limited to short-term erythema without signs of pathological inflammation, and the barrier properties of the epidermis are preserved. A clinically significant increase in surface smoothness is observed in the majority of patients. In particular, in the groups where mild enzymatic acids were used, in particular in cases of mandelic peeling, the proportion of individuals with maximum smoothness indicators reached more than 80%, while other organic agents showed lower, but still positive values. Evenness of skin tone and texture is most often observed in 70–100% of the participants in the procedures, and the preservation of a normal structure without signs of clinical lesions is recorded in all, which confirms the low risk of irritation compared to aggressive acid

approaches [2].

In patients with dehydrated or dry skin type, a high ability to improve elasticity and optical uniformity is maintained, however, in sensitive individuals, a single exacerbation of rashes is possible, as was recorded when using products with vitamin C, where the frequency of an adverse reaction did not exceed 40% in samples with specific sensitization. In models of oily and seborrheic skin, a decrease in the severity of relief defects, in particular closed comedones, is consistently recorded, which is associated with the effective separation of corneocytes in the surface layer without disturbing deeper structures [2].

Regarding clinical practice using a 2% aqueous solution of a supramolecular acid-enzyme complex, the results show changes in the main skin parameters over 28 days of use. Already on the 7th day, an increase in cheek gloss by +8.08% and a decrease in comedone volume by -16.25% are observed, which reflects the early normalization of desquamation and a decrease in follicular obstruction. By the end of the observation, the improvements become comprehensive: the hydration index increases by +25.0%, and water loss through the epidermis decreases by -6.86%, which indicates an increase in the barrier function [10].

Peeling preparations are also used as home remedies. If the formula is balanced and the temperature regime is observed, then the use of the preparation every evening for 28 days provides a gradual statistically significant improvement in the skin condition, which was manifested after the first application [5].

That is, the generalized clinical result over several sessions, in clinical conditions, is characterized by the transition of patients from average skin condition to the category of “excellent” clinical appearance, and it is this dynamic that is demonstrated by most temperature-activated enzymatic protocols [2].

The sequence of procedures is also important in the effectiveness of the drugs. It is important when the temperature-activated mild enzyme-acid peeling is built up step by step, that is, a system that is stored in a relatively “dormant” state in a jar and reveals its full exfoliating effect only under the conditions of the skin – its temperature and pH.

At the first level, the very concept of mild acid micropeeling is formed. The use

of a cream containing 4.5% of the AHA/BHA mixture and brown algae extract, the acid is laid in a low but pharmacologically active concentration, at a pH of about 3.6. This pH is sufficient to rupture corneodesmosomes, but does not create a deep chemical burn. The cream is intended for night use, so at the moment of application the formula goes from room temperature to the skin surface temperature and works for many hours at ~32–34 °C.

The second level is the actual technology of combining acids and proteases into a single supramolecular system. In the work on supramolecular acid–enzyme complex (SAE) [5] it is described that mandelic acid, betaine and a composite enzyme (papain + bromelain) are organized into a deep eutectic complex through a branched network of hydrogen bonds. Such a liquid "acid-enzyme salt" dramatically increases the solubility of proteases in water and at the same time shields them from denaturation, i.e. eliminates the classic problem of enzyme fragility in a cosmetic matrix. Comparative tests show that in this form the activity of papain/bromelain is preserved, and the ability of the complex to remove the stratum corneum in vitro exceeds both free enzymes and acid alone: SAE gives a more pronounced exfoliation of corneocytes at the same or lower doses. Clinically, a 2% aqueous solution of SAE, applied to the face for 4 weeks, demonstrates clearly quantitative effects: already on the 7th day, the gloss of the cheeks increases by about 8% and the volume of comedones decreases by ~16%, and after 28 days, the hydration of the stratum corneum increases by 25%, the gloss increases by almost 16% and the smoothness of the skin according to the SEsm parameter improves by about 8% [9].

The third level concerns temperature activation and the construction of a carrier in which the enzyme remains active but not destroyed throughout the entire shelf life. With a properly selected thickener (cellulose, xanthan gum or a combination thereof), most formulas retain activity at a level close to the calculated one even after 1–1.5 months, while the combination of the enzyme with certain UV filters and carbomers gives a lower starting level and a more noticeable loss of activity over time. Proteolytic enzymes in cosmetics are specifically selected so that their optimum falls on the temperature of the human body and the pH range of the skin; it is the transition from

storage conditions to the temperature and pH of the face that is considered a natural trigger for enzyme activation. The average pH values of the facial skin are indicated in the range of 4.7–5.9, and enzymes are described as “turning on” upon contact with this microenvironment, while too high or low pH and prolonged heating above the optimum reduce activity [6].

If we combine these three approaches, the technological process of temperature-activated enzymatic peeling will look like this in a simplified form: At the development stage, an acidic background with a low, clinically proven concentration of AHA/BHA is selected, which in itself provides micropeeling without gross barrier damage. In parallel, a protease with optimum activity in the skin temperature zone and weakly acidic–neutral pH (papain, bromelain) is selected, and this protease is stabilized either by a supramolecular eutectic network with acid and osmolyte (mandelic acid + betaine), or by a competently selected emulsion matrix with thickeners that do not inactivate the active center of the enzyme. During the application phase, the product is applied to the skin at its physiological temperature, and it is this temperature transition, together with the skin pH, that triggers the cascade: acids weaken the intercellular cement, and the protease, which has become more mobile and has reached its temperature optimum, hydrolyzes the protein components of the corneodesmosomes. Externally, this looks like a controlled “micropeeling” without intense erythema and edema, but with a quantitatively confirmed reduction in roughness, pore diameter, comedones, sebum production and an increase in hydration and barrier integrity, which is shown in clinical series for acid micropeeling and for the SAE complex [5].

As a result, the technological process of temperature-activated enzymatic peeling, as it is actually implemented in modern works, is not one “magic ingredient”, but a combination of three blocks: a mild acidic background, a structurally stabilized enzyme and a carrier, in which the enzyme activity is minimally lost during storage, but is maximally realized only at the temperature and pH of real skin. It is this design that makes it a non-irritating alternative to more aggressive methods of skin renewal.

Today, classical peeling methods are actively supplemented with combined technological solutions that integrate physical, chemical and bioactive factors of

influence on the stratum corneum. This approach allows for more precise control of the depth and direction of exfoliation, modulation of regenerative processes and minimizing damage to the epidermal barrier. One example is the author's Hollywood Facial Signature technique, developed by Oksana Zhenzherukha, which is based on the staged, gradual removal of displaced cells and synchronous restoration of the microstructure of the epidermis.

This protocol consists of ten consecutive stages. Each stage is aimed at a separate pathophysiological link in the formation of stratum corneum dysfunctions, and their combined application provides a synergistic effect:

1.Two-stage cleansing provides personalized removal of lipid and surface impurities in accordance with the individual skin condition map.

2.Enzyme exfoliation promotes delicate destruction of corneodesmosomes and removal of horny cells without irritation.

3.Microdermabrasion provides controlled abrasion to smooth the microrelief and improve skin permeability.

4.Hydrodermabrasion combines hardware cleansing with simultaneous infusion of active substances and tissue hydration.

5.Atraumatic extraction is aimed at eliminating comedonal formations with minimal trauma.

6.Oxygen mesotherapy promotes the delivery of bioactive serum components under the influence of a controlled flow of oxygen.

7.LED therapy modulates inflammatory reactions and stimulates reparative processes through the use of individually selected light spectra.

8.Hydrogel mask provides intensive moisture saturation and support of the barrier mechanisms of the epidermis.

9.Facial and shoulder girdle massage activates lymphatic drainage, normalizes microcirculation and improves muscle tone.

10.Final care using author's formulas contributes to prolonged maintenance of the result and photoprotection.

The technique is characterized by high adaptability to different skin types and is characterized by synergy of physical, chemical and bioactive mechanisms of action, which allows achieving a pronounced clinical effect without significant disruption of the epidermal barrier.

Conclusions

Thus, enzymatic peeling is based on natural mechanisms of desquamation, aimed at selective degradation of protein structures of the stratum corneum (primarily keratin and corneodesmosomes) that hold corneocytes in a dense intercellular matrix. Proteases of natural origin (papain, bromelain, keratinases) catalyze the hydrolysis of peptide bonds in extracellular horny masses without affecting viable cells, thereby ensuring delicate and controlled exfoliation without disrupting the barrier function of the epidermis.

Temperature-enzymatic peeling demonstrates a reproducible clinical effect. Its manifestations are visible from the first week: the gloss of the cheek increases by approximately +8%, and the volume of comedones decreases by −16%, which indicates an early normalization of desquamation. By the 28th day of use, a significant improvement in hydration at the level of +25% is recorded with a parallel decrease in transepidermal water loss by approximately −7%, which reflects an increase in the barrier function of the epidermis. The overall clinical assessment confirms that more than 80% of patients demonstrate a maximum increase in surface smoothness, while 70–100% - evenness of tone and texture without signs of pathological inflammation.

Modern peeling technologies are moving towards combined multimodal protocols, in which physical, chemical and bioactive factors are combined for controlled exfoliation and simultaneous restoration of the barrier and structural properties of the epidermis. An example is the multi-stage author's Hollywood Facial Signature technique by Oksana Zhenzherukha, which involves a sequential effect on various pathophysiological links in the formation of the stratum corneum and provides a synergistic result with high clinical efficacy and good tolerability for different skin types.

References

1. Białkowski K., Nowak P., Sokolowska M. Proteolytic activity of cosmetic enzyme peel products. Acta Biochimica Polonica, 2022, №69(4), 895–899. URL: https://doi.org/10.18388/abp.2020_6485

2. Dogiparthi S.N., Mohan S., Bala A., Jenson J. Effectiveness of various organic peels in facial rejuvenation and treatment of sensitive skin. Journal of Medical Science and Research, 2023, №11(4), 310–314. URL: http://dx.doi.org/10.17727/JMSR.2023/11-57

3. Encapsulated Enzymes: The Future of Gentle Yet Effective Exfoliation. flychem.com, 2025. URL: https://flychem.com/blogs/articles/encapsulated-enzymes-the-future-of-gentle-yet-effective-exfoliation?srsltid=AfmBOoobHU774WNkyGo9Mo60ZZhARlY-hJ-A-62FkA8eKm3vWwRSCvKw

4. Exfoliators & Scrub Market Size, Share, Growth, and Industry Analysis, By Type (Exfoliators, Scrub), By Application (Men, Women, Kids, Elder), Regional Insights and Forecast to 2034. marketgrowthreports.com, 2025. URL: https://www.marketgrowthreports.com/market-reports/exfoliators-scrub-market-110671

5. Namkoong J., Goswami S., Tartar O., Diaz I., Wu J. In-vitro efficacy investigation and an open-label, single-arm clinical study of a gentle micropeeling cream for sensitive and non-sensitive skin. Cosmetics, 2022, №9(6), 138. URL: https://doi.org/10.3390/cosmetics9060138

6. Torfgård K.E. Development and Evaluation of an Enzyme-Based Sunscreen. Lund University, 2023. URL: https://lup.lub.lu.se/luur/download?func=downloadFile&recordOId=9125069&fileOId=9127957

7. Trevisol T.C., Henriques R.O., Souza A.J.A., Furigo A. An overview of the use of proteolytic enzymes as exfoliating agents. Journal of Cosmetic Dermatology, 2022, №21(8), 3300–3307. URL: https://doi.org/10.1111/jocd.14673

8. Venetikidou M., Lykartsi E., Adamantidi T., Prokopiou V., Ofrydopoulou A.,

Letsiou S., Tsoupras A. Proteolytic enzyme activities of bromelain, ficin, and papain from fruit by-products and potential applications in sustainable and functional cosmetics for skincare. Applied Sciences, 2025, №15(5), 2637. URL: https://doi.org/10.3390/app15052637

9. Wójcik A., Kubiak M., Rotsztejn H. Influence of azelaic and mandelic acid peels on sebum secretion in ageing women. Adv Dermatol Allergol/Postępy Dermatol i Alergol, 2013, №30(3), 140-145. URL: https://doi.org/10.5114/pdia.2013.35614

10. Zhou H., Zhang W., Li X., Li R., Dong C., Tang L. Development and clinical evaluation of a supramolecular acid–enzyme complex for controlled skin exfoliation. Journal of Dermatologic Science and Cosmetic Technology, 2025, №2(3), 100109. URL: https://doi.org/10.1016/j.jdsct.2025.100109