

Platelet-Rich Autologous Plasma in Complex Treatment of Sutton Aphthae: Clinical, Immunological and Cytomorphological Outcomes

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Abstract Objective: to assess the clinical, immunological, microbiological and cytomorphological efficacy of local platelet-rich autologous plasma (PRP) injections as an adjunct to conventional therapy for Sutton aphthae. Methods: an open-label randomized controlled study included 112 patients aged 25–60 years with severe scarring recurrent aphthous stomatitis. Conventional treatment was given to 53 patients; 59 patients additionally received 4–5 perilesional PRP injections. Lesion area, disease severity, OHIP-14-RU, salivary TNF- α , IL-2, IL-10 and lactoferrin, oral microbiota, local defense factors and cytology were evaluated through day 29 and at 90 and 180 days. Results: by day 22 the lesion area decreased to $1.90 \pm 2.23 \text{ mm}^2$ with PRP versus $6.24 \pm 1.83 \text{ mm}^2$ after conventional therapy; complete epithelialization was documented from day 29 only in the PRP group. Clinical recovery reached 49.1% versus 28.3%, recurrence frequency was 15.8% versus 76.5%, and remission duration was 7.66 ± 0.27 versus 4.59 ± 0.15 months. After PRP-assisted therapy, TNF- α and IL-2 decreased to 6.88 ± 0.64 and $12.2 \pm 1.11 \text{ pg/mL}$, while IL-10 increased to $7.91 \pm 0.87 \text{ pg/mL}$. Lysozyme, phagocytic activity and sIgA approached control values, and cytology demonstrated epithelial restoration with minimal neutrophilic infiltration. Conclusion: local PRP accelerated repair, rebalanced the local inflammatory response and reduced recurrence activity without procedure-related adverse events.

Keywords Sutton aphthae, major recurrent aphthous stomatitis, platelet-rich plasma, cytokines, oral immunity, epithelial repair

1. Introduction

Recurrent aphthous stomatitis is among the most frequent inflammatory disorders of the oral mucosa. Its clinical spectrum ranges from small superficial ulcers that heal without scarring to deep, persistent defects that interfere with eating, speech and sleep. Sutton aphthae represent the major scarring phenotype: lesions are commonly larger than 10 mm, painful, slow to epithelialize and prone to relapse [1,2].

The pathogenesis is multifactorial. T-cell dysregulation, a pro-inflammatory cytokine shift, altered oral microbiota, reduced secretory defense and epithelial-barrier injury interact within the ulcer bed. Active disease is characterized by increased TNF- α and IL-2 with insufficient IL-10 activity; this pattern sustains neutrophil recruitment, delays epithelial proliferation and prolongs tissue destruction [3,13]. Elevated salivary lactoferrin additionally marks neutrophil activation and strain on nonspecific antimicrobial defense [15].

Conventional local therapy combines analgesia, enzymatic debridement, antiseptic treatment and keratoplastic agents. Although this approach reduces inflammation, large scarring ulcers may still heal slowly and relapse within several months. A regenerative adjunct is therefore attractive when the therapeutic goal is not only symptom control but also structured restoration of the epithelial barrier.

Platelet-rich autologous plasma provides a concentrated, patient-derived mixture of PDGF, TGF- β , VEGF, EGF, fibronectin and other bioactive mediators. These components support fibroblast and epithelial-cell migration, neoangiogenesis and extracellular-matrix remodeling [4–8]. PRP is well established in oral surgery, implantology and periodontology, whereas evidence for erosive-ulcerative mucosal disease remains limited [9–12]. The present study therefore evaluated whether early clinical improvement is accompanied by immunological normalization and cytomorphological repair.

The aim was to determine the clinical, immunological, microbiological and cytomorphological efficacy of perilesional PRP injections as part of complex treatment for Sutton aphthae.

2. Material and Research Methods

The open-label randomized controlled study was performed from 2020 to 2023 at an outpatient therapeutic-dentistry clinic. The cohort included 112 patients aged 25–60 years (mean age 46.7 ± 1.45 years); 45 were men and 67 were women. The comparison group comprised 53 patients treated conventionally, and the PRP group comprised 59 patients who received the same regimen supplemented by local autologous plasma injections. A laboratory subcohort included 45 patients and 15 practically healthy controls.

Eligible participants had clinically verified major scarring recurrent aphthous stomatitis, deep painful ulcers larger than 10 mm and a usual epithelialization period of at least 25–30 days. Pregnancy, lactation, age below 18 years, severe comorbidity and recent hormonal or immunocorrective therapy were exclusion criteria. All participants provided informed consent.

Both groups underwent oral sanitation, professional hygiene and correction of individual oral care. Conventional local therapy included topical analgesia, crystalline trypsin debridement, 0.05% chlorhexidine, Holisal gel and Solcoseryl dental adhesive paste. In the intervention group, PRP was injected around the ulcer margins after preparation of the lesion surface. Four to five procedures were performed according to the epithelialization rate.

Table 1. Study design, treatment arms and assessment schedule

Component	Treatment group		Timing / endpoint
	Conventional (n=53)	PRP-assisted (n=59)	
Treatment	Holisal + Solcoseryl DAP	Same regimen + PRP	4–5 perilesional injections
Clinical	Lesion area, pain, severity	Same outcomes	Days 1–29; 90 and 180 days
Quality of life	OHIP-14-RU	OHIP-14-RU	Baseline, day 21, month 3
Immunology	TNF- α , IL-2, IL-10	Same panel	Before and after therapy
Local defense	Lysozyme, phagocytosis, sIgA	Same panel	Before and after therapy

Clinical examinations were performed on days 1, 3, 5, 7, 12, 17, 22 and 29, followed by visits at 90 and 180 days. Ulcer area was calculated as an irregular ellipse, $S = (\pi \times d_1 \times d_2) / 4$. Disease severity and OHIP-14-RU were recorded. Unstimulated saliva was collected in the morning; TNF- α , IL-2 and IL-10 were determined by enzyme-linked immunoassay, and lactoferrin by an immunological method. Microbiological analysis used serial dilution and selective culture with results expressed as lg CFU/mL. Local resistance was assessed from lysozyme, neutrophil phagocytic activity and secretory IgA. Cytological smears and scrapings were stained by Romanowsky–Giemsa, Papanicolaou or hematoxylin–eosin.

Quantitative data are presented as mean $\pm$ standard error. Differences were considered statistically significant at $p < 0.05$. Interpretation emphasized concordance between clinical, immunological, microbiological and cytological changes.

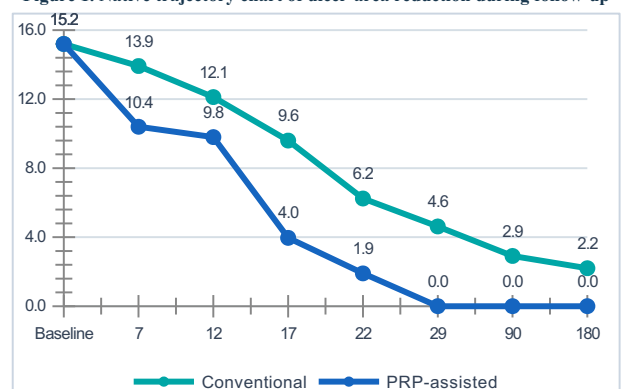
3. Results

3.1. Ulcer Healing and Early Clinical Response

At baseline, the groups were clinically comparable. Patients had deep crater-like ulcers with fibrinonecrotic coating, hyperemic infiltrated margins and severe pain; exacerbations occurred five to six times per year. Mean baseline lesion area was $15.2 \pm 2.20 \text{ mm}^2$.

The lesion began to contract after the first PRP injections. In the intervention group, area decreased to $10.40 \pm 1.01 \text{ mm}^2$ on day 7, $9.80 \pm 1.60 \text{ mm}^2$ on day 12, $3.96 \pm 2.42 \text{ mm}^2$ on day 17 and $1.90 \pm 2.23 \text{ mm}^2$ on day 22. Complete epithelialization was recorded from day 29. Conventional therapy produced a slower trajectory: lesion area remained $9.60 \pm 1.72 \text{ mm}^2$ on day 17, $6.24 \pm 1.83 \text{ mm}^2$ on day 22 and $4.62 \pm 1.11 \text{ mm}^2$ on day 29, with residual defects at 90 and 180 days.

Figure 1. Native trajectory chart of ulcer-area reduction during follow-up



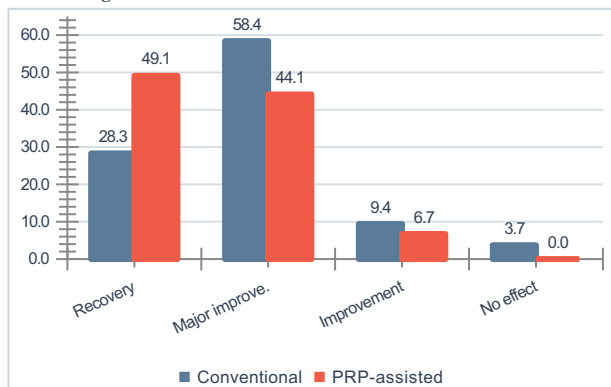
Values are mean lesion area (mm²). The chart is an editable native Word object with embedded Excel data.

The PRP effect extended beyond lesion size. By day 3, general-condition scores, low-grade fever and regional lymphadenitis decreased more rapidly. By day 5, the disease-severity index fell from 1.72 ± 0.10 to 0.68 ± 0.05 in the PRP group versus 1.17 ± 0.10 after conventional therapy.

3.2. Clinical Effectiveness, Quality of Life and Relapse

Final clinical outcomes differed substantially. Clinical recovery occurred in 49.1% of PRP-treated patients versus 28.3% after conventional treatment. Significant improvement was recorded in 44.1% and 58.4%, respectively; no-effect cases were observed only in the comparison group (3.7%).

Figure 2. Native clustered chart of final clinical outcomes



Bars represent the percentage of patients in each response category. Data labels and source sheet remain editable.

Table 2. Clinical and long-term outcomes with a two-tier treatment header

Outcome	Treatment group		PRP effect
	Conventional	PRP-assisted	
Clinical recovery	28.3%	49.1%	+20.8 percentage points
Residual area, day 29	$4.62 \pm 1.11 \text{ mm}^2$	0 mm^2	Complete epithelialization
Recurrence frequency	76.5%	15.8%	-60.7 percentage points
Remission after therapy	$4.59 \pm 0.15 \text{ mo}$	$7.66 \pm 0.27 \text{ mo}^*$	+3.07 months
OHIP-14-RU, month 3	24.6 ± 0.34	$14.3 \pm 0.19^*$	-10.3 points

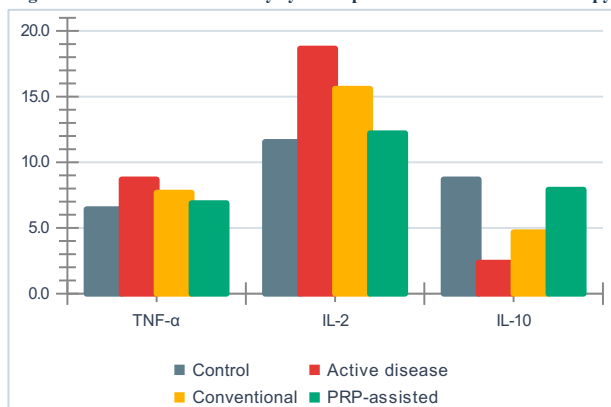
*Statistically significant versus conventional therapy, $p < 0.05-0.01$, according to the source dataset.

OHIP-14-RU scores were similar before treatment (34.6 ± 0.95 and 35.1 ± 0.38). By day 21 they decreased to 24.4 ± 0.38 with conventional therapy and to 11.7 ± 0.34 with PRP ($p < 0.05$). The advantage persisted at three months. Recurrence frequency was 76.5% versus 15.8%; the mean number of recurrences per patient was 1.88 ± 0.12 versus 0.88 ± 0.01 , and the next-exacerbation severity index was 1.62 versus 0.92.

3.3. Cytokine Rebalancing

Active Sutton aphthae were accompanied by a distinct local inflammatory shift. Salivary TNF- α increased to $8.69 \pm 0.66 \text{ pg/mL}$ and IL-2 to $18.65 \pm 1.62 \text{ pg/mL}$, whereas IL-10 fell to $2.35 \pm 0.36 \text{ pg/mL}$. Conventional therapy moved these mediators in a favorable direction but did not restore the physiological range. After PRP-assisted treatment, TNF- α was $6.88 \pm 0.64 \text{ pg/mL}$, IL-2 was $12.2 \pm 1.11 \text{ pg/mL}$ and IL-10 increased to $7.91 \pm 0.87 \text{ pg/mL}$.

Figure 3. Native chart of salivary cytokine profiles before and after therapy



Control, active disease, post-conventional therapy and post-PRP profiles are displayed as editable series.

Table 3. Salivary cytokine profile, pg/mL

Marker	Healthy control	Active disease	After treatment	
			Conventional	PRP-assisted
TNF- α	6.42 ± 0.68	$8.69 \pm 0.66^*$	7.68 ± 0.35	6.88 ± 0.64
IL-2	11.54 ± 2.39	$18.65 \pm 1.62^*$	15.6 ± 0.98	12.2 ± 1.11
IL-10	8.69 ± 0.49	$2.35 \pm 0.36^*$	4.66 ± 0.38	7.91 ± 0.87

* $p < 0.05$ versus healthy control.

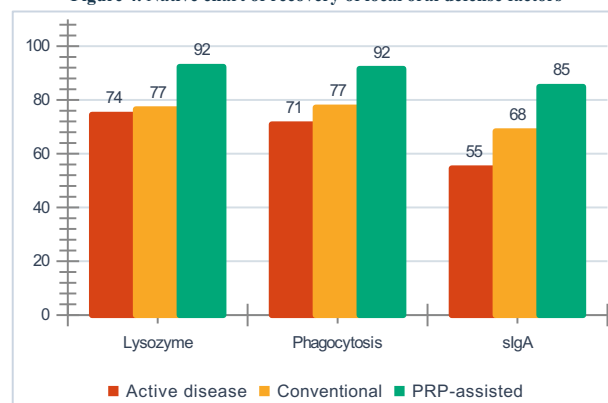
At baseline, TNF- α correlated directly with IL-2, while both mediators correlated inversely with IL-10. The reduction in ulcer area paralleled the decline in pro-inflammatory mediators, supporting cytokine monitoring as an objective adjunct when pain relief precedes complete epithelial restoration.

3.4. Oral Microbiota and Local Resistance

The initial microbiota profile showed depletion of anaerobes and lactobacilli with expansion of facultative opportunistic flora. Total anaerobes decreased from 6.30 ± 0.44 to $4.56 \pm 0.42 \text{ lg CFU/mL}$ and lactobacilli from 5.75 ± 0.34 to $3.15 \pm 0.40 \text{ lg CFU/mL}$, while aerobes increased from 4.65 ± 0.29 to $6.45 \pm 0.45 \text{ lg CFU/mL}$. Staphylococcus aureus, S. epidermidis, Streptococcus mutans, Proteus and Candida spp. were frequently isolated.

Local defense was simultaneously impaired. Lysozyme, neutrophil phagocytosis and sIgA were 74%, 71% and 55% of control values before treatment. Conventional therapy produced modest recovery, whereas PRP-assisted treatment restored the same factors to approximately 92%, 92% and 85% of control.

Figure 4. Native chart of recovery of local oral defense factors



Values are normalized to healthy control = 100%. The chart is fully editable in Word.

Table 4. Local oral-defense factors

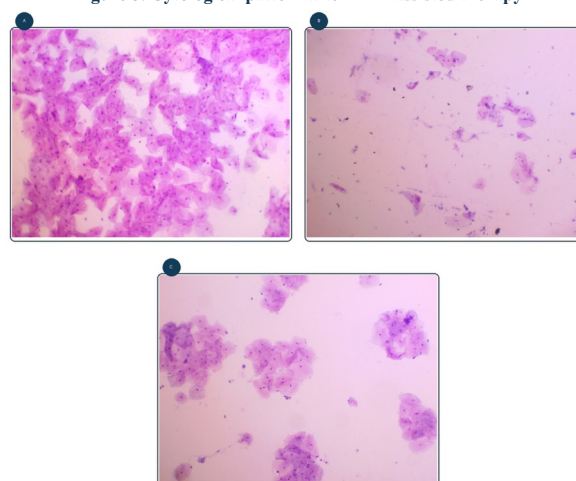
Factor	Healthy control	Active disease	After treatment	
			Conventional	PRP-assisted
Lysozyme, mg%	19.6 ± 1.44	14.6 ± 1.2	15.0 ± 0.4	18.1 ± 0.5
Phagocytosis, %	55.7 ± 3.34	39.5 ± 2.44	43.0 ± 1.5	51.0 ± 2.1
sIgA, g/L	2.18 ± 0.13	1.19 ± 0.13	1.49 ± 0.10	1.85 ± 0.10

Improvement in local resistance was accompanied by recovery of anaerobic flora and lactobacilli and a reduction in excessive aerobic colonization. The changes were not uniform for every species, indicating that PRP does not replace oral sanitation or plaque control; rather, it may support barrier recovery within a comprehensive program.

3.5. Cytomorphological Repair and Safety

Before treatment, smears contained desquamated and necrotic tissue, diffuse neutrophil aggregates, erythrocytes and mucus, with only isolated squamous epithelial cells. Epithelial dystrophy and necrobiosis included cytoplasmic vacuolization, nuclear pyknosis and fragmentation. After complex therapy, neutrophilic infiltration markedly decreased, necrotic material disappeared or remained as isolated fragments, and preserved squamous epithelial cells predominated. Mild nuclear enlargement with a regular membrane and homogeneous chromatin was interpreted as reparative hypertrophy without atypia.

Figure 5. Cytological pattern after PRP-assisted therapy



A — preserved buccal epithelial cells; B — isolated epithelial cells with minimal inflammatory infiltration; C — epithelial clusters without necrotic material.

No complications related to venipuncture or local PRP injection were registered. One early recurrence in the PRP group was associated with dietary nonadherence; treatment continued after behavioral correction.

3.6. Practical Outpatient Protocol

The applied pathway links diagnostic verification, lesion preparation, regenerative intervention and long-term control. It is intended for large, deep, slowly epithelializing ulcers with frequent relapse and substantial quality-of-life impairment.

Table 5. Practical algorithm for PRP-assisted management of Sutton aphthae

Stage	Clinical pathway	
	Action	Control point
1	Verify Sutton aphtha and exclude systemic ulcerative disease	Clinical diagnosis and risk profile
2	Oral sanitation, hygiene and removal of mechanical trauma	Clean lesion surface and stable hygiene
3	Analgesia, trypsin debridement, chlorhexidine, Holisal and Solcoseryl DAP	Reduced inflammation and prepared ulcer bed
4	Perilesional PRP according to healing rate	Four to five procedures
5	Review on days 7–29 and at 90/180 days	Area, severity, OHIP-14-RU and relapse

4. Discussion

The study yielded a coherent clinical-laboratory model of treatment response. Pain and inflammatory symptoms improved first, followed by granulation, rapid contraction of the ulcer defect and complete epithelialization. In parallel, TNF-α and IL-2 decreased, IL-10 recovered, and lysozyme, phagocytosis and sIgA approached physiological values. The final cytological transition from a necrotic-neutrophilic pattern to epithelial repair reduces the likelihood that the observed benefit was limited to topical analgesia.

The effect is biologically plausible. Holisal suppresses local inflammatory activity, and Solcoseryl DAP protects the ulcer surface and supports epithelialization. PRP adds an autologous pool of growth factors and matrix proteins. PDGF and TGF-β regulate cell migration and proliferation, VEGF supports neovascularization and EGF accelerates epithelial restoration [4–8]. A coordinated mixture of mediators may better reproduce the physiological sequence of wound healing than a single recombinant factor.

The rise in IL-10 is especially relevant. Major recurrent aphthous stomatitis is associated with a Th1-oriented response; low IL-10 permits persistent production of pro-inflammatory mediators and delays epithelial proliferation [3,13]. In the PRP group, IL-10 approached the healthy range, matching the reduction in neutrophilic infiltration and disappearance of necrotic material.

Microbiota findings should be interpreted cautiously. PRP is not an antimicrobial drug. The more favorable microbial profile most likely resulted from sanitation, improved epithelial-barrier integrity, higher lysozyme and sIgA, and elimination of the ulcer niche. The method should therefore remain an adjunct within complete oral care rather than an isolated injection procedure.

The strongest clinical relevance emerged during follow-up. Remission length increased by more than three months, and recurrence frequency decreased by 60.7 percentage points. OHIP-14-RU remained lower at three months, indicating that early epithelialization translated into sustained improvements in eating, speech, rest and social interaction.

Several limitations require consideration. The study was single-center and open-label; immunological and microbiological analyses were performed in a specialized subcohort, follow-up was limited to 180 days, and platelet concentration was not standardized for each PRP preparation. Multicenter studies with platelet-dose characterization and follow-up of at least 12 months are needed.

5. Conclusions

- 1. Perilesional PRP accelerated reduction of Sutton aphtha area and produced complete epithelialization by day 29, whereas a residual defect persisted after conventional therapy.
- 2. PRP-assisted therapy improved clinical recovery, OHIP-14-RU and remission duration and substantially reduced recurrence frequency without procedure-related adverse events.
- 3. The treatment shifted the salivary cytokine profile toward physiological values and restored lysozyme, neutrophil phagocytosis and secretory IgA.
- 4. Cytology confirmed true epithelial repair through disappearance of necrotic material, reduction of neutrophilic infiltration and restoration of squamous epithelial structure.
- 5. The method is most justified for large, deep, slowly healing and frequently recurrent aphthae within a structured outpatient protocol that includes sanitation, debridement and follow-up.

REFERENCES

[1] Preeti L, Magesh KT, Rajkumar K, Karthik R. Recurrent aphthous stomatitis. *J Oral Maxillofac Pathol.* 2011;15(3):252–256. doi:10.4103/0973-029X.86669.

[2] Tappuni AR, Kovacevic T, Shirlaw PJ, Challacombe SJ. Clinical assessment of disease severity in recurrent aphthous stomatitis. *J Oral Pathol Med.* 2013;42(8):635–641. doi:10.1111/jop.12059.

[3] Teng F, Jin Q. Evaluation of cytokine expressions in patients with recurrent aphthous stomatitis: a systematic review and meta-analysis. *PLoS One.* 2024;19(6):e0305355. doi:10.1371/journal.pone.0305355.

[4] Marx RE. Platelet-rich plasma: evidence to support its use. *J Oral Maxillofac Surg.* 2004;62(4):489–496. doi:10.1016/j.joms.2003.12.003.

[5] El-Sharkawy H, Kantarci A, Deady J, et al. Platelet-rich plasma: growth factors and pro- and anti-inflammatory properties. *J Periodontol.* 2007;78(4):661–669. doi:10.1902/jop.2007.060302.

[6] Barrientos S, Stojadinovic O, Golinko MS, Brem H, Tomic-Canic M. Growth factors and cytokines in wound healing. *Wound Repair Regen.* 2008;16(5):585–601. doi:10.1111/j.1524-475X.2008.00410.x.

[7] Foster TE, Puskas BL, Mandelbaum BR, et al. Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med.* 2009;37(11):2259–2272. doi:10.1177/0363546509349921.

[8] Boswell SG, Cole BJ, Sundman EA, et al. Platelet-rich plasma: a milieu of bioactive factors. *Arthroscopy.* 2012;28(3):429–439. doi:10.1016/j.arthro.2011.10.018.

[9] Mazzocca AD, McCarthy MB, Chowanec DM, et al. Platelet-rich plasma differs according to preparation method and human variability. *J Bone Joint Surg Am.* 2012;94(4):308–316. doi:10.2106/JBJS.K.00430.

[10] Makedonova IA, Firsova IV, Temkin ES, et al. Justification of the effectiveness of Plasmolifting procedure in patients with erosive and ulcerative lesions of the oral cavity. *Res J Med Sci.* 2016;10(3):64–68.

[11] Usmanova LB, Kamilov KhP. Prospects for the use of plasmolifting in dentistry. *Uzbek Medical Journal.* 2022;6–11. doi:10.5281/zenodo.7394692.

[12] Kamilov Kh, Usmanova L, Akhmadaliev NN. Dynamics of the cytokine profile of oral fluid in patients with Sutton aphthosis. *Uzbek Medical Journal.* 2023;67–73. doi:10.5281/zenodo.7800556.

[13] Ghasemi S, et al. Systematic review and meta-analysis of oxidative stress and antioxidant markers in recurrent aphthous stomatitis. *BMC Oral Health.* 2023;23:960. doi:10.1186/s12903-023-03636-1.

[14] Liu H, Tan L, Fu G, Chen L, Tan H. Efficacy of topical intervention for recurrent aphthous stomatitis: a network meta-analysis. *Medicina.* 2022;58(6):771. doi:10.3390/medicina58060771.

[15] Berluti F, Pilloni A, Pietropaoli M, Polimeni A, Valenti P. Lactoferrin and oral diseases: current status and perspective. *Ann Stomatol (Roma).* 2011;2(3–4):8–10.

[16] Usmanova LB, Kamilov KhP. Development and evaluation of the effectiveness of complex treatment for Sutton aphthae. *Medical Journal of Uzbekistan.* 2026;(2):45–48. doi:10.64156/mju.8969.

[17] Kamilov KhP, Shukurova UA. Clinical assessment of chronic aphthous stomatitis using the overall severity index: methodological recommendations. Tashkent; 2008. 16 p.