



# Development And Evaluation of The Efficiency of Ointment for Cheilitis Treatment in Patients with Dental and Jaw Anomalies

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## ABSTRACT

*Cheilitis is a group of chronic diseases of the vermillion border that are diverse in etiology, pathogenesis and clinical picture. The development of various forms of cheilitis is facilitated by defects of the architectonics of the lips, unhealthy lifestyle, anatomical features of the lip structure, adverse meteorological effects, decrease in specific and non-specific factors for protecting the oral cavity, the patient's psycho-emotional state, immuno-allergic factors and accompanying general somatic and dental pathologies. The issues of prevention and comprehensive treatment of lip diseases are especially relevant in dental practice. The article presents data on the prevalence of cheilitis and dentoalveolar anomalies and the need for their treatment in young people. Furthermore, the authors provide a composition justification and develop an ointment for the treatment of cheilitis in this category of patients.*

**Keywords:** cheilitis, dentoalveolar anomalies, ointment, young people.

## INTRODUCTION

Young people as the basis of the future require increased attention from the state and healthcare system in particular. The health status of students who form this age category as an important social group of Russian society is not only an indicator of the existing socio-economic and social development of the country but also an important indicator of the future labor, economic, cultural and defense potential of society [1]. Various social programs aimed at

strengthening and maintaining health and forming a healthy lifestyle have become more widespread in Russia recently.

Dental status is one of the main indicators of the general condition of the body, and the development of a system of measures aimed at reducing the incidence of dental morbidity should be an integral part of programs to improve the nation's health condition [2]. Dentoalveolar anomalies are one of the components that form the dental status of an individual, thereby determining the general condition of the body. Orthodontic pathology can indirectly become one of the etiological factors in the development of diseases of both dental and other organs and systems. The prevalence rates of dentoalveolar anomalies are inferior to caries and share second place with periodontal diseases. This pattern can be traced for several decades in studies conducted both in Russia and abroad and in some regions, there is a tendency to increase. An analysis of the observations of dentists around the world shows that more than 80% of the world's population under 25 years of age have anomalous tooth arrangement, expressed to a certain degree. From 35 to 60% of these patients require the intervention of an orthodontist [3-12].

One of the conditions that usually accompany dentoalveolar anomalies is cheilitis. Cheilitis is a group of chronic diseases of the vermillion border that are diverse in etiology, pathogenesis and clinical picture.

The prevalence of certain types of chronic, often recurring independent diseases of the vermillion border among

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various population groups varies widely — from 3.9 to 26.4% [13-15]. The most common are inflammatory and destructive diseases, such as meteorological, exfoliative and actinic cheilitis and chronic lip cracks [16, 17].

The etiology of cheilitis is diverse. Cheilitis can occur under the influence of external causes (traumatic, meteorological, chemical) and internal factors (genetic predisposition). Typical allergens causing cheilitis are foods, medications, pollen, household dust, microorganisms, ingredients of toothpaste, lipstick and cosmetics [18-23]. Cheilitis is the result of the combined effects of adverse exogenous and endogenous stimuli. In the development of cheilitis, a determining, but not the only factor is a lip architectonics defect. The second and indispensable prerequisite is the unhealthy state of the integumentary tissues, such as skin, vermilion border and mucous membrane, and their inadequate response to the influence of the external environment [24]. The integrity of the human body, as well as the interdependence of the form and functions of its organs and systems, is confirmed by the study of the relationship between local and general disorders of the body arising from dentition anomalies. The most common signs of cheilitis are oral breathing and dentoalveolar abnormalities [25].

Cheilitis is not regarded by doctors as a serious process and rarely attracts special attention of researchers. However, it has a significant impact on the well-being and social activity of patients. The presence and severity of lip diseases, including cheilitis, have a significant impact on the patient's quality of life [26]. Despite a wide range of anti-inflammatory medications, the treatment of inflammatory lip diseases requires the development of new medications. The medications used must provide an antimicrobial, wound healing and keratoplastic effect and also

contain a minimum amount of synthetic chemicals.

## METHODS

We conducted a dental examination of 1,398 people aged from 16 to 25 years. We studied the prevalence of dentoalveolar anomalies and the need for their treatment and the prevalence of lip diseases.

The antioxidant activity of medicinal plant materials was determined by spectrophotometry based on autooxidation of adrenaline at 347 nm. Water extracts from the studied plants and their mixtures were introduced into the model system, in which the reactions of autooxidation of adrenaline in a buffer solution at pH = 12 were generated and proceeded. The absorption spectra were measured using a SHIMADZU UV-1800 instrument. We used a 0.5% solution of ascorbic acid as the comparator.

The wound healing activity of the ointment for the treatment of cheilitis was studied on outbred female rats weighing 260 g. The rats were anesthetized with urethane. Patchwork wounds were reproduced by cutting a skin flap to remove subcutaneous tissue in a previously shaved area (right side) using a stencil [27]. The animals were divided into three groups (n = 8): the control group (the wound was treated with ointment base — beeswax and vegetable oil in a ratio of 3: 7), the experimental group (ointment for the treatment of cheilitis containing an oil extract based on the fruits of mountain ash, marigold flowers, thyme as the active substance) and the comparator (Kamistad (Stada, Germany)). Treatment was started the day after wound reproduction. The ointment, the base and the reference preparation were applied directly to the wounds once a day until they healed. On the 1st, 7th, 10th and 13th days, the size of the wounds was traced on film.



The surface area of the wounds was calculated using the formula:  $S = \frac{\pi}{4}(x^2 + y^2)$ , where  $x$  and  $y$  are wound diameters (mm). The wound healing process was judged by the decrease in the average surface area of the wounds in groups compared to the initial data.

The anti-inflammatory activity of the ointment for the treatment of cheilitis was studied on 30 white outbred male and female mice weighing 18-22 g. The animals were divided into four groups: the intact control group, the ointment base control group (beeswax and vegetable oil in a ratio of 3: 7), the experimental group treated with ointment (the ointment for the treatment of cheilitis, containing an oil extract based on fruits of mountain ash, marigold flowers, thyme grass as the active substances and Diclofenac comparator group (Voltaren Emulgel 1%, Novartis, Switzerland). Further, the animals of the corresponding group had ointment for the treatment of cheilitis, the ointment base or Voltaren applied to their left paw for seven days; the intact control group simulated the application of ointment. On the 7th day, the ointment was applied twice (2 hours and 1 hour) before the reproduction of the edema. Acute edema was caused by the introduction of 0.05 ml of a 1% carrageenin solution under the plantar aponeurosis of the left hind paw, the right paw served as a control. Three hours after the induction of inflammation, the mice were taken out of the experiment using diethyl ether, the paws were cut off in the ankle joint and weighed [28]. The severity of edema was judged by the difference between the experimental and the healthy paw; the results were expressed as a percentage. The anti-inflammatory effect of the extract was evaluated by the ability to reduce edema relative to the control; the results were expressed as a percentage.

The study of the clinical effectiveness of the ointment was attended by 24

people aged 18 to 23 years. We revealed dentoalveolar anomalies of varying severity and need for treatment in all participants. The main group consisted of 12 people (meteorological cheilitis, chronic lip fissure), for whom we used an ointment based on an oil extract of a collection of medicinal plants containing fruits of mountain ash, marigold flowers and thyme grass as a topical medicine. The comparison group consisted of 12 people who applied Kamistad gel topically.

The objective of the study was to develop and evaluate the effectiveness of an ointment for the treatment of cheilitis in young people with dentoalveolar anomalies.

## RESULTS AND DISCUSSION

The total prevalence of dentoalveolar anomalies amounted to 83.12% (83.43% among females and 82.26% among males). The structure of dentoalveolar anomalies was as follows: anomalies of individual teeth were diagnosed in 5.51% of participants, anomalies of the dentition in 22.72% of participants, anomalies of occlusion were observed in 6.54% of participants, combined anomalies were recorded in 65.23% of participants.

When studying the prevalence of dentoalveolar anomalies, only the fact of their presence is recorded, which does not give a complete picture of this problem, and also does not reflect the severity of the anomalies and the need for treatment. For these purposes, we used the DAI aesthetic dental index recommended by the WHO (Cons, 1986). We also evaluated the dental health component (DHC) of the index of orthodontic treatment need (IOTN) (Shaw & Evans, 1987).

Indicators of the DAI aesthetic index below 25 indicating the presence of minimal malocclusion were identified



in 78.54% of participants. DAI values of 26–30 are interpreted as a clear malocclusion, which requires selective treatment, identified in 13.73% of students. According to the results of the study, DAI values from 31 to 35 characteristic of severe malocclusion are found in 4.86% of young people. DAI indicators of 36 and higher determining the presence of very severe malocclusion and requiring compulsory treatment were observed in 2.86%.

According to the interpretation of the indicators of the DHC component of the IOTN index, 31.69% of participants did not need treatment (grade 1) and 44.85% had a low need (grade 2). We determined an average/borderline degree of need for treatment in 15.74% of young people (grade 3); 6.58% of participants had a high need (grade 4) and only 1.14% — a very high need for orthodontic treatment (grade 5).

Lip pathology was diagnosed in 23.8% of participants. Biting cheeks was detected in 3.9%. Leukoplakia, lichen planus and other pathologies were detected in 2.2% of cases. Cheilitis was diagnosed in 13.4% of participants. Meteorological cheilitis prevailed (9.8%), chronic lip cracks were recorded in 2.9%. Cases of actinic, atopic and exfoliative cheilitis were recorded in 0.7% of participants. Most often, cheilitis was detected in those examined with combined dentoalveolar anomalies (16.89%) and occlusion anomalies (14.47%). In participants without dentition anomalies, the prevalence of cheilitis equaled 1.7%.

As a result of the study, nasal breathing disorders were detected in 22.99% of cases and the infantile type of swallowing was observed in 10.69% of participants diagnosed with cheilitis. Anomalies in the attachment of soft tissues were recorded in 21.39% of young people. Periodontal disease was detected in 89.3% of participants. An allergic history with complications was observed in 17.64% of participants.

Smoking is also a factor in the development of cheilitis. According to the questionnaire, the number of young smokers suffering from cheilitis is 20.32%, with 43.58% of males and 14.19% of females. According to the questionnaire and the survey, the unhealthy habit of licking or biting the lips was observed in 16.58% of participants, 33.33% and 12.16% in males and females respectively.

We developed an ointment for the treatment of cheilitis, which included an oil extract of medicinal plants as the active substance and beeswax as the base. The oil extract was obtained from the collection of medicinal plants containing the fruits of common mountain ash, calendula flowers and thyme grass in equal proportions, with the ratio of collection and sunflower oil 1: 6 and the ratio of ointment base and oil extract 3: 7. Beeswax is a mixture of esters of high molecular weight alcohols with palmitic acid. The 3: 7 ratio of beeswax and oil extract allows to obtain a hydrophobic ointment, which provides a pronounced prolonged therapeutic activity.

To justify the composition, we studied the antioxidant properties of each component separately and in a mixture. As a result of the study, it turned out that the infusion of thyme grass in the studied concentrations did not have antioxidant activity and the infusion of calendula flowers and decoction of rowan fruits had weak antioxidant activity, reducing the autooxidation of adrenaline by an average of  $14.5 \pm 0.7\%$  and  $12.6 \pm 0.6\%$ , respectively. The comparator (0.5% ascorbic acid solution) had an antioxidant activity of  $39.9 \pm 1.6\%$ . According to the method used, the obtained values of more than 10% indicate the presence of antioxidant activity in the studied objects. When measuring the antioxidant activity of the mixture of the studied components (calendula flowers, thyme and rowan fruits), it turned out that the studied composition





reduced the autooxidation of adrenaline by an average of  $28.9 \pm 1.6\%$ , which indicated the potentiation of the pharmacological effect in the joint presence of several types of medicinal plant materials and increased antioxidant activity.

According to an experiment conducted to evaluate the wound healing activity of the ointment, during the first three days, we noted swelling of the edges of the wounds, soreness; the animals were inactive. By the 7th day of treatment, the area of wounds in groups compared with the initial data decreased. Thus, in the control group and the comparator group, the wound area decreased by 74.4% ( $P = 0.028$ ) and 74.5% ( $P = 0.018$ ), in the experimental group — by 68.8% ( $P = 0.028$ ). By the 10th day of treatment, suppuration of wounds was observed in two animals of the control group and the average area decreased by 84.1% ( $p = 0.028$ ). In the experimental group and the comparator group, wound healing was more active, with the area decreasing by 91.2% ( $p = 0.028$ ) and 94.1% ( $p = 0.018$ ), respectively, compared with the initial values. In the ointment group, the area of wounds was two times smaller than that of the control group ( $p > 0.05$ ). By the 10th day, in the Kamistad comparator group, the area of the wounds was less than in the ointment group ( $p > 0.05$ ) and the base group ( $p = 0.038$ ). By the 13th day of treatment, complete wound healing was observed in the comparator groups and almost all animals of the experimental and control groups. In the experimental group, there was only one animal with a wound with an area of  $15.7 \text{ mm}^2$ , and in the control group, there were two such animals with the wound area of  $50.2 \text{ mm}^2$  and  $8.2 \text{ mm}^2$ . The wounds were clean, shallow without swelling at the edges.

The anti-inflammatory effect of the test ointment was evaluated by the ability to reduce edema caused by the introduction of a 1% carrageenin solution. In the

control group, the weight gain of the inflamed paw ( $69.0 \pm 6.4 \text{ g}$ ) and the severity of edema ( $47.5 \pm 3.5\%$ ) were maximal, compared with the rest of the groups. The anti-inflammatory activity of the base, ointment and Voltaren comparator was 12%, 16%, and 20% compared to the control group ( $p > 0.05$ ).

The developed ointment was tested on patients with dentoalveolar anomalies and cheilitis. Patients complained about dry and burning lips and pain when opening the mouth, talking and eating. The ointment for the treatment of cheilitis was used as follows: it was applied to the surface of the lips with a thin layer three times a day and held on the lips for one hour. The effectiveness of the treatment technique was evaluated according to the following criteria: positive dynamics of clinical manifestations, reduction in the duration of treatment of patients by 2-3 visits in the main group compared with the group, in which Kamistad gel was used, and improvement in the quality of life (interviewing with the OHIP-14 RU questionnaire on the profile of the impact of dental health). Conducting therapy using a treatment for cheilitis reduced the treatment time to 10-14 days, depending on the timing of contacting a doctor from the onset of the disease. A day after the use of the medication, pain and itching stopped and hyperemia and edema decreased. Epithelization of the affected surface of the lips occurred on the 10th-14th day.

## CONCLUSION

The study of the prevalence of dentoalveolar anomalies, the need for their treatment, the prevalence of cheilitis in young people led to the development of an ointment for the treatment of cheilitis in patients with dentoalveolar anomalies, consisting of an oil extract of medicinal plants as the active substance



and beeswax as the base with pronounced antioxidant, wound healing and anti-inflammatory effects, as well as helping to reduce treatment time. The developed ointment can be recommended as a medication for treating cheilitis in young people with dentoalveolar anomalies.

## REFERENCES

1. Zhuravleva, I.V. Zdorove studentov: sotsiologicheskii analiz [Student health: a sociological analysis]. Institute of Sociology of the Russian Academy of Sciences. Moscow, pp. 252, 2012.
2. Khoshchevskaya, I.A. Organizatsiya i printsipy raboty shkolnogo stomatologicheskogo kabineta v sovremennykh usloviyakh [Organization and principles of work of a school dental office in modern conditions]: Avtoref. dis. ... kand. med. nauk [Author's abstract of a cand. med. sci. dissertation]. Moscow, 2010.
3. Averyanov, S.V., Iskhakov, I.R., Isaeva, A.I., Garaeva, K.L. Rasprostranennost i intensivnost kariessa zubov, zabolevanii parodontita i zubochehyustnykh anomalii u detei goroda Ufy [The prevalence and intensity of dental caries, periodontal diseases and dentoalveolar anomalies in children of the city of Ufa]. *Sovremennye problemy nauki i obrazovaniya*, 2, pp. 114, 2016.
4. Gileva, E.S. Sistemnyi analiz parametrov makro- i mikroestetiki ulybki u lits molodogo vozrasta i ego dinamika v protsesse lecheniya skuchennogo polozheniya zubov vo frontal'nom otdele: avtoref. dis. kand. med. nauk [System analysis of the parameters of macro- and microaesthetics of a smile in young people and its dynamics in the treatment of crowded teeth in the front: author's abstract of a cand. med. sci. dissertation]. Perm, pp. 22, 2007.
5. Glukhova, Yu.M., Shpak, N.S. Izuchenie nuzhdaemosti naseleniya Khabarovska v ortodonticheskoy lechenii s pomoshchyu estheticheskikh indeksov [The study of the need of orthodontic treatment in the population of Khabarovsk using aesthetic indices]. *Institut stomatologii*, 1(46), pp. 24-25, 2010.
6. Doroshina, V.Yu., Makeeva, I.M., Protsenko, A.S. Stomatologicheskaya dispanserizatsiya studentov Moskovskikh VUZov i puti povysheniya ee effektivnosti [Dental medical examination of students of Moscow universities and ways to increase its effectiveness]. *Stomatologiya*, 1(7), pp. 9, 2010.
7. Kuroedova, V.D., Makarova, A.N. Rasprostranennost zubochehyustnykh anomalii u vzroslykh i dolya asimmetrichnykh form sredi nikh [The prevalence of dentoalveolar anomalies in adults and the proportion of asymmetric forms among them]. *SMB*, 4, pp. 31-35.
8. Maksimova, E.M. Izuchenie zabolevaemosti i urovnya okazaniya lechebno-profilakticheskoi stomatologicheskoi pomoshchi naseleniyu Stavropolskogo kraia: avtoref. diss.kand.med.nauk [The study of the incidence and level of medical and preventive dental care for the population of the Stavropol region: author's abstract of a cand. med. sci. dissertation]. Moscow, pp. 23, 2007.
9. Ogonyan, E.A. Effektivnost dispanserizatsii studentov s zubochehyustnymi anomaliyami i deformatsiyami: avtoref. diss. kand.med. nauk [The effectiveness of medical examination of students with dentoalveolar anomalies and deformities: author's abstract of a cand. med. sci. dissertation]. Volgograd, pp. 23, 2011.

10. Manin, A.I. Rasprostranennost anomalii zubov u zhibelei razlichnykh regionov Rossii [The prevalence of tooth abnormalities in residents of various regions of Russia]. *Ortodontiya*, 1(25), 2004, pp. 9-12.
11. Hassan, A.H. Orthodontic treatment needs in the western region of Saudi Arabia: a research report. *Head & Face Medicine*, 2(2), 2006.
12. Uçüncü, N., Ertugay, E. The use of the Index of Orthodontic Treatment need (IOTN) in a school population and referred population. *J Orthod.*, 28(1), pp. 45-52, 2001.
13. Banchenko, G.V., Kryazheva, S.S. Sochetannye porazheniya slizistoi obolochki polosti rta i kozhi [Combined lesions of the mucous membrane of the oral cavity and skin]. *Atlas*. Moscow, pp. 160, 2004.
14. Mashkileison, A.L., Kutin, S.A., Zalkiev, R.N. Klinika kheilitov v dermatologii i venerologii [Clinical symptoms of cheilitis in dermatology and venereology]. Moscow, 1983.
15. Rabinovich, I.M., Alimskii, A.V., Toidzhakova, D.D. Rasprostranennost zabolevanii slizistoi obolochki polosti rta u rabotnikov khlopko-pererabatyvayushchei promyshlennosti [The prevalence of diseases of the oral mucous membrane in cotton workers]. *Stomatologiya*, 4, pp. 61-64, 2008.
16. Alimskii, A.V. Meteorologicheskie kheility – kraevaya patologiya severnykh promyshlennykh territorii [Meteorological cheilitis — a regional pathology of the northern industrial territories]. *Novoe v stomatologii*, 2(82), pp. 35-36, 2000.
17. Kulygina, V.N. Patogeneticheskoe obosnovanie kompleksnogo lecheniya i profilaktiki vospalitelnykh i destruktivnykh zabolevanii krasnoi kaimy gub [Pathogenetic substantiation of complex treatment and prevention of inflammatory and destructive diseases of the vermilion border]: Avtoref. dis. ... dokt. med. nauk [Author's abstract of a cand. med. sci. dissertation]. Kiev, pp. 49, 2004.
18. Barer, G.M. *Terapevticheskaya stomatologiya* [Therapeutic dentistry]. Moscow: GEOTAR-Media, 2005.
19. Masyukova, S.A. Vliyanie klimaticheskikh uslovii na barernye svoistva kozhi krasnoi kaimy gub [The influence of climatic conditions on the barrier properties of the skin of the vermilion border]. *Eksperimentalnaya i klinicheskaya dermatokosmetologiya*, 3, pp. 22-27, 2010.
20. Asai, M., Kawada, A., Aragane, Y., Tezuka, T. Allergic contact cheilitis due to glyceryl monoisostearate monomyristate in a lipstick. *Contact Dermatitis*, 45(3), pp. 173, 2001.
21. Corazza, M., Levratti, A., Virgili, A. Allergic contact cheilitis due to carvone in toothpastes. *Contact Dermatitis*, 46(6), pp. 366-367, 2002.
22. Guin, J.D. Allergic contact cheilitis from di-isostearyl malate in lipstick. *Contact Dermatitis*, 44(6), pp. 375, 2001.
23. Park, K.K., Brodell, R.T., Helms, S.E. Angular cheilitis, part 1: local etiologies. *Cutis*, 87(6), pp. 289-295, 2011.
24. Rylov, A.V. Zdorove nashikh gub [The health of our lips]. *Bud zdorov*, 5, pp. 18-22, 2011.
25. Rusakova, E.Yu. Rasprostranennost i intensivnost zubocheilyustnykh anomalii u detei shkolnogo vozrasta s razlichnymi somaticheskimi zabolevaniyami [The prevalence and intensity of dentoalveolar anomalies in schoolchildren with various somatic diseases]. *Klinicheskaya stomatologiya*, 1, pp. 62-65, 2011.



26. Averyanov, S.V., Romeiko, I.V. Vliyaniye kheilitov na kachestvo zhizni studentov [The influence of cheilitis on the students' quality of life]. *Sovremennye problemy nauki i obrazovaniya*, 3, pp. 222, 2015.
27. Frolova, N.Yu. Metodicheskie podkhody k eksperimentalnomu izucheniyu dermatotropnykh sredstv [Methodological approaches to the experimental study of dermatotropic medications]. *EKF*, 72(5), pp. 56-60, 2009.
28. Mironov, A.N. Rukovodstvo po provedeniyu doklinicheskikh issledovaniy lekarstvennykh sredstv. Chast pervaya [Guidelines for pre-clinical studies of medications. Part one]. Moscow: Grif i K, pp. 944, 2012.