

## Article

# Effect of antioxidant dental gel on the adaptation of the oral mucosa to removable dentures.

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**Abstract:** Determination of the effect of a gel with natural astaxanthin on the timing of adaptation of the oral mucosa to removable dentures. The gel made from a natural antioxidant reduces the risk of stomatitis, values of hygienic indices and traumatic factor. **Aims:** Reduction of the period of adaptation to removable dentures in patients with partial adentia. The objective was to evaluate the effect of antioxidant gel on the oral mucosa. **Patients and Methods.** The state of oropharyngeal microbiocenosis was studied in 105 patients aged 30-65 years old who were divided into three groups: the main group - 45 patients; comparison group - 35 patients; control group - 25 patients. The groups were comparable by age; gender differences were not taken into account. Patients in the main group received astaxanthin gel for 7 days after the delivery of the removable denture. Patients in the comparison group did not receive astaxanthin gel after the delivery of the removable denture. Clinical indices were used to assess oral hygiene: oral hygiene index plaque index API, gingivitis index, papillary-marginal-alveolar - (PMA); gingival sulcus bleeding index - SBI. We used a therapeutic and prophylactic agent in the form of a gel containing natural astaxanthin - 0.026%, vitamin E - 2.2%, Coenzyme Q - 1.5%. **Result.** According to the results of the analysis of the visual control and the results of photometric registration of the speed of healing and adaptation of the patient to the prosthesis, the data obtained differed in the patients of the 1st and 2nd groups. Visual control data of the dynamics of inflammatory changes in the oral mucosa development, received by the results of semi-quantitative evaluation of the severity of edema and hyperemia indicate significant differences in the rate of their reduction depending on the type of the applied tactics. In the case of group 1, prophylactic gel was applied from the time of denture fitting, and in group 2, only denture correction was performed. Thus, the index of hyperemia intensity testified to the disappearance of signs of the latter in Group 1 (gel with natural astaxanthin) - by the 4th day of observation, in Group 2 - by the 10th day after prosthesis correction. Complete disappearance of the signs of edema, respectively, was ascertained: in Group 1 - on the 4-5th day of observation and in Group 2 - by the 10th-11th day, at that, edema was retained 1-2 days longer. The method of photoplanimetric registration of the healing rate objectively confirmed the results obtained. **Conclusion.** Studies of the effectiveness of the gel containing natural astaxanthin indicate improved oral hygiene parameters of patients and reduced concentration of bacterial endotoxin and plasmalogen metabolites of oral microorganisms after 7 days of using the gel. Prophylactic dental gel with astaxanthin reduces the rate of adaptation to removable dentures by 1.7 - 2 times and reduces the risk of denture stomatitis due to wound healing, anti-inflammatory and anti-microbial action.



**Keywords:** natural astaxanthin, partially removable denture, hyperemia, anti-inflammatory effect, antioxidant.

## 1. Introduction

The purpose of this clinical study: to determine the terms of adaptation of oral mucosa to removable dentures on the normalization of basic hygienic and biochemical indicators when using the therapeutic and prophylactic agent in the form of a gel with natural astaxanthin. The task was set: to evaluate the effectiveness of antioxidant gel application in patients with partial secondary adentia.

Protection against oxidation and cell destruction in the body belongs to antioxidants. However, under certain conditions almost all of them turn into pro-oxidants and begin to harm the body by increasing the oxidation process. Inside the body, free radicals harm tissues and the immune system by destroying cells and DNA structure [1]. Universal adaptogens include antioxidants, so they are used in the treatment and prevention of diseases of the oral mucosa [2, 3].

Natural astaxanthin, due to the peculiarity of its biochemical structure, is the most powerful antioxidant that does not turn into a pro-oxidant [4, 5, 6]. It has prolonged anti-inflammatory and immunomodulatory effects. Its positive use in the treatment of cardiovascular diseases and cancer is known [7, 8].

The oral mucosa has good protective and barrier functions in response to the various mechanical and traumatic lesions to which it is exposed. However, when exposed to mechanical traumatic lesions of greater force, some changes occur [9]. The response to various stimuli in the oral mucosa depends on the nature, strength, duration and duration of the provocative factor. When exposed to any traumatic agent there is a response in the form of inflammation [10, 11, 12].

Traumatic denture stomatitis is common in dental practice. The complaints of patients with denture stomatitis are pain in the area of the denture bed at the site of injury, which increases when using dentures [1, 2]. The causes of this pathology may include poor workmanship, the presence of roughness of the denture. Single roughnesses and pores in the base of a removable denture can also cause focal inflammatory processes in the oral mucosa. A limited catarrhal inflammation of the oral mucosa occurs if the denture is used for a short period of time. If the traumatic factor is not eliminated, swelling and hyperemia will occur, which may lead to the subsequent formation of erosions. With prolonged exposure to the traumatic factor, ulcers can develop on the oral mucosa. The key to the successful treatment of traumatic denture stomatitis is the timely correction of the dentures and the absence of signs of inflammatory diseases of the oral mucosa [7, 13].

Modern medicine focuses on preventive measures aimed at regulating the balance of the oral microflora, and stimulating natural protective mechanisms to eliminate pathogenic agents [1]. So in the majority of therapeutic and prophylactic means for oral care, manufacturers already include antiseptics of a wide spectrum of action: triclosan, chlorhexidine and others. These components are included in most hygiene products of different forms of use: toothpaste, gels, balms and rinses [14, 15, 16]. Given the advertising and promotional activities on television and radio broadcasts, these products are among those widely used and dominate among the rest. However, it should be taken into account that despite the success of the above antiseptics in the correction of oral microbiocenosis, the literature data also indicate their adverse effect on the composition of oral fluid microbiota [17].

It was found that natural astaxanthin contributes to the regulation of oral microbiocenosis, having anti-inflammatory, antimicrobial, wound-healing effect [18]. On the basis of this natural antioxidant was made dental gel to reduce the period of adaptation to removable dentures, as well as the prevention of denture stomatitis oral cavity. The action of astaxanthin is enhanced by vitamin E and coenzyme Q [12].

## 2. Aims

Reduction of the period of adaptation to removable dentures in patients with partial adentia. The objective was to evaluate the effect of antioxidant gel on the oral mucosa.

## 3. Materials and methods

The state of oropharyngeal microbiocenosis was studied in 105 patients aged 30-65 years old who were divided into three groups: the main group - 45 patients; comparison group - 35 patients; control group - 25 patients. The groups were comparable by age; gender differences were not taken into account. Patients in the main group received astaxanthin gel for 7 days after the delivery of the removable denture. Patients in the comparison group did not receive astaxanthin gel after the delivery of the removable denture. The inclusion criteria for the control group were patients with



one or two metal-free crowns, no removable dentures, no signs of periodontal and oral mucosal inflammation, and no dental anomalies or deformities. Patients with cancer, immunodeficiency diseases, diabetes mellitus and severe somatic condition, as well as smokers and pregnant women were excluded from the study.

Clinical indices were used to assess oral hygiene: oral hygiene index plaque index API, gingivitis index, papillary-marginal-alveolar - (PMA); gingival sulcus bleeding index - SBI [3]. The calculation was performed according to the methods of index calculation by the authors of the indices [1].

The state of oropharyngeal microbiocenosis was assessed according to the concentrations of bacterial plasmalogens and endotoxin determined by gas chromatography mass spectrometry of saliva [13].

We used a therapeutic and prophylactic agent in the form of a gel containing natural astaxanthin - 0.026%, vitamin E - 2.2%, Coenzyme Q - 1.5% (RF patent No 2599026 "Composition for healing tissues in the oral cavity" Bulletin No 28 of 8.09.2016 Declaration of compliance, main registration number: 1037739230979. Oral hygiene product "Astadent", compliance with TU 20.42.18-001-28910991-2017).

Examination of the patients' oral cavity, as well as oral fluid analyses to determine the concentrations of small molecules by gas chromatography mass spectrometry were taken at 3 stages of the study: Stage 1 - before gel application, Stage 2 - after 7 days of gel exposure, Stage 3 - after 28 days of gel application.

The evaluation of clinical manifestations in the oral cavity in patients of the main group (group 1) and group 2 after the application of partial dentures in the oral cavity was carried out.

The 45 patients of group 1 (21 female, 24 male, 25 immediate dentures and 20 removable partial dentures), who received the gel within 7 days from the first day of placing the removable denture, had hyperemia of the denture bed in 86.6% of cases and edema in 55.6% of patients with immediate dentures, erosions were not observed. The 20 patients with partial dentures showed hyperemia in 70% of cases and edema in 25% of cases, no erosions were observed.

Oral pigmentary state was also studied using API, PMA and SBI indices in group 1-3 patients on days 1, 7, 28 of the study and concentrations of bacterial plasmalogens and bacterial endotoxin were studied by gas chromatography and mass spectrometry.

The incidence of morphological types of complications in 35 patients in group 2 during the primary application of removable prosthesis directly due to the irritating mechanical impact on the oral mucosa was in 17 patients with immediate prosthesis (100% cases) and in the majority of patients with plate prosthesis (94.4% of cases). At the same time, hyperemia and edema were also more pronounced and erosions were more frequent in patients with immediate prostheses. Erosions occurred in 71.4% of cases.

At each examination, a visual assessment of the state of the oral mucosa and prosthetic bed tissues was performed, and if indicated, the design was corrected. The intensity of inflammation in the erosion or ulcer zone was assessed according to two parameters: the degree of swelling and hyperemia.

We used a semi-quantitative method to assess a particular manifestation, which consisted in assigning one of 5 conditional ranks (points) to each degree of the observed changes: 0, no corresponding change; 1.0, weak degree of its manifestation; 2.0, moderate degree; 3.0, strong degree; and 4.0, very strong degree. The evaluation was made before the beginning of the prosthesis and at time points: 2, 4, 6, 8, and 10 days. The data obtained in each selected group were averaged, and the mean values obtained were used in further statistical analysis.

Photo-planimetric control of hyperemia reduction was determined by taking photographs of the prosthetic bed at their standard magnification. A point planimetric grid of 49 points was superimposed on the photographs. By counting the number of points per wound surface and comparing this index with the previous result, the percentage of the healing rate of the oral mucosa in the dynamics was determined. Photographs were taken with a digital camera Nikon D60, lens - sigma 24 -70 mm f2.8 EX DG Macro with the subsequent grid overlay in the Photoshop CC photo editor before the placement of the removable prosthesis and at the time of: 2, 4, 6, 8 and 10 days.

#### 4. Research results and their discussion

A positive prophylactic and anti-inflammatory effect of astaxanthin gel was established in patients with immediate and partial removable dentures. Application of the gel in the short term at the stage of 7 days contributes to a decrease in the values of hygiene indices, concentrations of bacterial plasmalogen and endotoxin in the oral fluid.

According to the results of the analysis of the visual control and the results of photometric registration of the speed of healing and adaptation of the patient to the prosthesis, the data obtained differed in the patients of the 1st and 2nd groups. Visual control data of the dynamics of inflammatory changes in the oral mucosa development, received by the results of semi-quantitative evaluation of the severity of edema and hyperemia indicate significant differences in the rate of



their reduction depending on the type of the applied tactics. In the case of group 1, prophylactic gel was applied from the time of denture fitting, and in group 2, only denture correction was performed. Thus, the index of hyperemia intensity testified to the disappearance of signs of the latter in Group 1 (gel with natural astaxanthin) - by the 4th day of observation, in Group 2 - by the 10th day after prosthesis correction. Complete disappearance of the signs of edema, respectively, was ascertained: in Group 1 - on the 4-5th day of observation and in Group 2 - by the 10th-11th day, at that, edema was retained 1-2 days longer. The method of photoplanimetric registration of the healing rate objectively confirmed the results obtained.

In addition, the evaluation of clinical manifestations in the oral cavity of the patients of the main group (group 1) and group 2 after the application of partial dentures in the oral cavity was carried out. Comparative data are presented in Table 1.

Table 1. Prevalence of clinical manifestations in the prosthetic bed area after the delivery of a partial denture. \* - reliability  $P \leq 0.05$ .

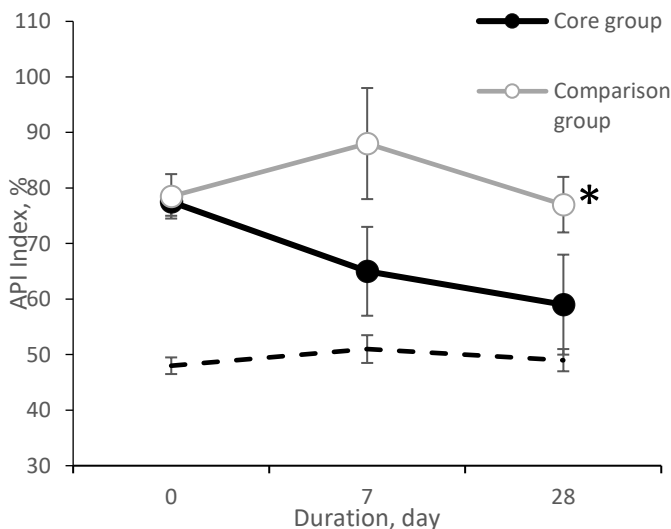
Symptoms	Group 1 (n=45)	Group 2 (n=35)
Hyperemia	39 (86,6%)	35 (100%)
Swelling	25 (55,6%)	34 (97,1%)
Erosion	0	25 (71,4%)

According to the data shown in Table 1, we can conclude that the clinical manifestations and complaints in the oral cavity of patients in Group 1 with the use of prophylactic gel based on natural astaxanthin, which proves the preventive effect of dental gel and the lack of need for correction of dentures. Patients in Group 2 required correction in the first week after placing removable dentures.

The evaluation of the effectiveness of the gel in terms of changes in the hygienic state of the oral cavity is presented in Fig. 1,2,3. Figure 1 shows the average values of API index for 1,2 and group 3 (G.C.) and at 3 stages of the study: before gel application, 7, 28 days after gel application.

Table 2. API index in patients at different stages of the study.

API Index, %	Averages		
	Core group	Comparison group	Control group
Duration, day			
0	77,5	78,5	48
7	65	88	51
28	59	77	49



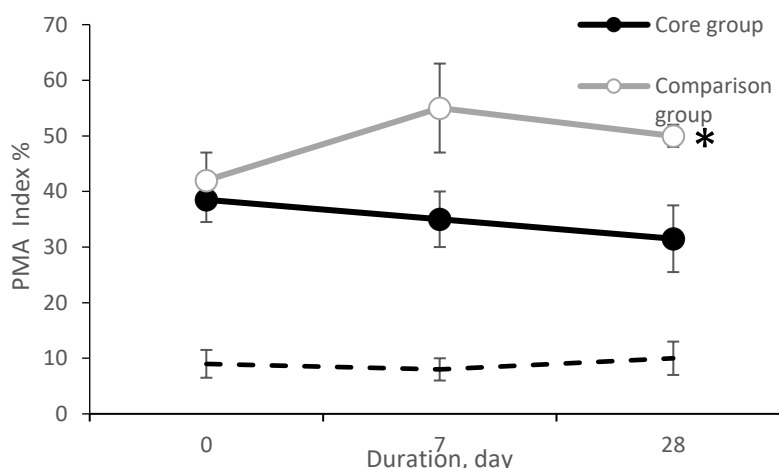
**Figure 1.** API index in patients at different stages of the study. \* - significant difference in the group relative to the 1st stage of the study,  $p < 0.05$ .

Figure 1 shows that in the main group there is a value of the API index exceeding the value of 70% - the boundary of unsatisfactory state of the mouth at the initial stage before treatment and reliably exceeding the average values of the indices in comparison group patients. In 7 and 28 days after using the gel a tendency to a decrease of API index values to the area of values characterizing satisfactory state of the mouth cavity was observed in the patients of the main group. Group 2 patients' API did not change significantly. Thus, the positive influence of the gel on the hygienic state of the mouth cavity in the part of the dental plaque is noted.

Changes in the index of oral gingivitis in patients before and after using the gel is shown in Fig. 2.

**Table 3.** PMA index in patients at all stages of research.

PMA Index, %	Averages		
	Core group	Comparison group	Control group
Duration, day			
0	38,5	42	9
7	35	55	8
28	31,5	50	10



**Figure 2.** PMA index in patients at different stages of the study. \* - reliable difference in the group in comparison with the 1st stage of the study,  $p < 0,05$ .

There was a PMA index value characterizing unsatisfactory periodontal condition (40-60%) in Group 1 and 2 patients before the study. The PMA index values in all groups increased in groups 1 and 2, compared to group 3. As a result of using the gel, there was a tendency for the index to decrease on days 7 and 28 in the main group. In group 2, the PMA index values did not change significantly.

The follow-up results in group 1 compare the PMA values with those in group 3 and have a reliable difference with the initial value in their group.

Changes in the SBI hygiene index (gingival sulcus bleeding) in patients of the main groups and comparison group (GC) before and after the use of the gel are shown in Figure 3.

**Table 4.** SBI index in patients at all stages of the study.

SBI Index, %	Averages		
	Core group	Comparison group	Control group
Duration, day			
0	2	2	0
7	1	2,5	0



28	0,5	2	0
Scatter			
0	0,9	0,5	0
7	0,8	0,5	0
28	0,5	0,4	0

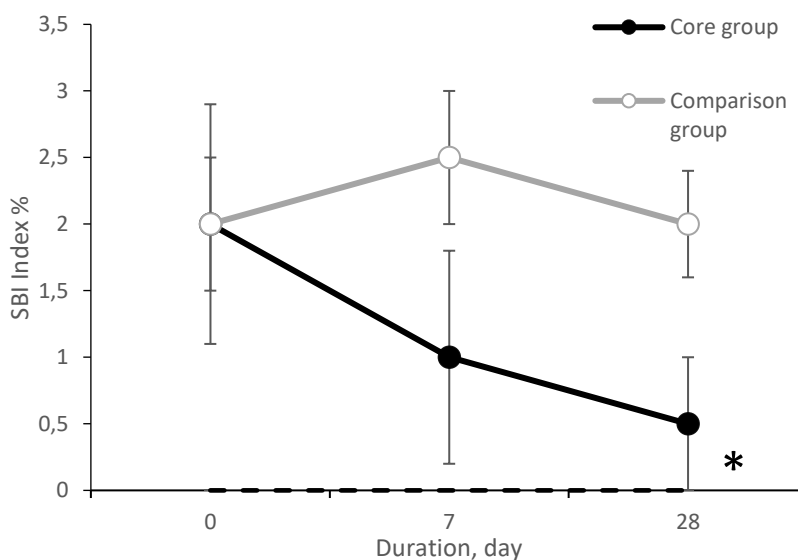


Figure 3. Bleeding index in patients at different stages of the study. \* - a significant difference in the group relative to the 1st stage of the study,  $p < 0,05$

In the 1 (main) group SBI index values had a significant difference from the 2 and 3 groups. In the main group there was a tendency to reduce the SBI values after the application of the gel. Thus, the obtained data indicate the absence of bleeding during probing.

Changes of plasmalogen and endotoxin concentrations by gas chromatography mass spectrometry in the oral liquid of the patients of the 1st (main) group and comparison group are shown in Figures 4 and 5.

Table 5. The concentration of bacterial plasmalogen in patients at all stages of the study.

Plasmalogen, mg/ml	Averages		
	Core group	Comparison group	Control group
Duration, day			
0	5,64	5,2	0,83
7	0,22	6,2	0,92
28	0,21	5,5	0,88
Scatter			
0	2	2	0,5
7	0,2	2,2	0,5
28	0,15	2,4	0,5



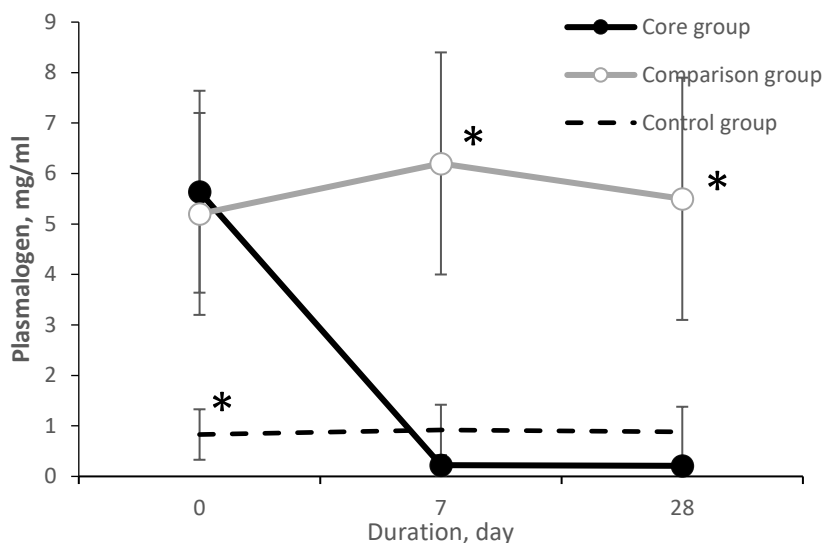


Figure 4. Concentration of bacterial plasmalogen in oral fluid in patients of groups 1, 2 and 3.\* - significant difference in the group relative to the 1st stage of the study, p<0.05.

Table 6. The concentration of bacterial endotoxin in patients at all stages of the study.

Endotoxin, nanomole/ml	Averages		
	Core group	Comparison group	Control group
Duration, day			
0	3,56	3,5	0,48
7	0,79	3,9	0,52
28	1,01	3,8	0,55
Scatter			
0	1	0,6	0,2
7	0,5	0,8	0,15
28	0,5	0,5	0,2

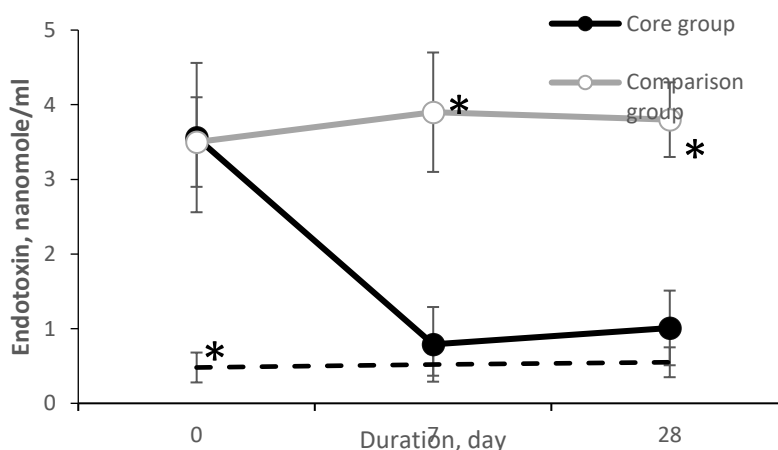


Figure 5. Concentration of bacterial endotoxin in oral fluid in patients of groups 1, 2 and 3.\* - significant difference in the group relative to the 1st stage of the study, p<0.05.

The graphs in Figure 4 show that the concentration of bacterial plasmalogen in the oral fluid of patients in groups 1 and 2 is increased relative to normal (50mcg/ml). In group 1, the concentration of bacterial plasmalogen in the oral fluid decreases and remains low on days 7, 28. The decrease



in the concentration of bacterial plasmalogen in the oral fluid immediately after the start of the gel can be explained by the antiseptic action of the gel component - astaxanthin. In group 2 the concentration of bacterial plasmalogen does not change statistically.

As a result of using the gel, the activity of the oral microflora decreases, which leads to a decrease in the concentration of plasmalogen in the oral fluid, with a constant concentration of plasmalogen in the blood. Similar trends in the concentration of bacterial endotoxin in the oral fluid can be noted after 7 days in patients 1 (main) group in the graphs shown in Fig. 5.

Changes in the concentration of bacterial endotoxin in the oral fluid are also explained by the local antiseptic action of astaxanthin. The tendency to a decrease in the concentration of bacterial endotoxin in oral fluid is an indirect indication of a decrease in the intensity of microbial infestation of the oral cavity, indicating a positive anti-inflammatory effect of natural astaxanthin.

The findings of the study are consistent with the literature on the mechanism of action and antimicrobial properties of natural astaxanthin. The mediated anti-inflammatory mechanism of action is the inhibition of cyclooxygenase 1 enzyme, neutralization of free radicals in mitochondria, suppression of inflammatory mediators such as: Tumor necrosis factor, Prostaglandin, interleukins, etc. [16-18].

## 5. Conclusion

Prophylactic dental gel with astaxanthin reduces the rate of adaptation to removable dentures by 1.7 - 2 times and reduces the risk of denture stomatitis due to wound healing, anti-inflammatory and antimicrobial action.

Thus, the study confirmed the positive prophylactic and anti-inflammatory effects of astaxanthin gel in patients with imediated and partial removable dentures. The application of the gel in the short-term at the stage of 7 days contributes to the reduction of values of hygiene indices, concentrations of bacterial plasmalogen and endotoxin in the oral fluid of group 1 patients. Index of hyperemia intensity, testified to the disappearance of inflammation signs in Group 1 (gel with natural astaxanthin) - by the 4th day of observation, in Group 2 - by the 10th day after denture correction. Complete disappearance of the signs of edema, respectively, was found: in Group 1 - on the 4-7th day of observation and in Group 2 - by the 10th-11th day, moreover, edema retained for 3-5 days longer. The method of photoplanimetric registration of the healing rate objectively confirmed the results obtained.

Studies of the effectiveness of the gel containing natural astaxanthin indicate improved oral hygiene parameters of patients and reduced concentration of bacterial endotoxin and plasmalogen metabolites of oral microorganisms after 7 days of using the gel. Prophylactic dental gel with astaxanthin reduces the rate of adaptation to removable dentures by 1.7 - 2 times and reduces the risk of denture stomatitis due to wound healing, anti-inflammatory and antimicrobial action.

**Conflicts of Interest:** The authors declare no conflict of interest

## References

1. Baidakova GV, Bukina AM, Goncharov, VM. Diagnosis of inherited metabolic diseases based on a combination of tandem mass spectrometry and enzymodiagnosics. *Medical Genetics* 2005; 4(1):28-32 (In Russian.).
2. Borovsky EV, Leontiev VK, Therapeutic stomatology. Moscow: Medical Information Agency 2004; 17 (In Russian).
3. Capelli B, Talbott S, Ding L. Astaxanthin sources: suitability for human health and nutrition *Functional Foods in Health and Disease* 2019; 9(6): 430-445.
4. Danciuk NV, Minyuk GS, Drobetskaya IV, Chubchikova IN, Chelebieva ES. Green microalgae *Haemotococcus pluvialis* as a renewed source of natural astaxanthin. *Marine biological research: achievements and prospects* 2016; 3:370-373 (In Russian).
5. Dong LY, Jin J, Lu G, Kang XL. Astaxanthin attenuates the apoptosis of retinal ganglion cells in db/db mice by inhibition of oxidative stress. *Marine Drugs* 2013; 11(5):960-974.
6. Grudyanov AI, Zorina OA. Diagnostic methods of inflammatory periodontal diseases: a guide for physicians. M: Medical Information Agency 2009; 112 (In Russian).
7. Hama S, Takahashi K, Inai Y, Shiota K, Sakamoto R, Yamada A, Tsuchiya H, Kanamura K, Yamashita E, Kogure K. Protective effects of topical application of a poorly soluble antioxidant astaxanthin liposomal formulation on ultraviolet-induced skin damage. *Journal of Pharmaceutical Sciences* 2012; 101:2909-2916.
8. Wu H, Niu H, Shao A, Wu C, Dixon BJ, Zhang J, Yang S, Wang Y. Astaxanthin as a Potential Neuroprotective Agent for Neurological Diseases 2015; 03:5750 - 5766.
9. Ishiki MY, Nishida H, Ishibashi T, Wada S, Fujisaka S, Takikawa A, Urakaze M, Sasaoka T, Usui I, Tobe K. Impact of divergent effects of astaxanthin on insulin signaling in I6 cells. *Endocrinology* 2013; 154:2600-2612.
10. Karkishchenko NI, Pyrimidines NI, Karkishchenko ZhK. *Aslanyants. Pharmacology and toxicology* 1989; 6(52):100-103 (In Russian).
11. Lobeiko VV, Iordanishvili AK, Kuvshinova AK. Treatment of prosthetic traumatic stomatitis. In the collection: current issues of stomatology. collection of scientific works, dedicated to the founder of the department of orthopedic stomatology of kgm professor Isaak Mikhailovich Oxman. Kazan 2018; 225-230 (In Russian).
12. Onishchenko GG, Alyoshkin VA, Afanasiev SS, Pospelova VV. Immunobiological preparations and prospects for their use in infectiology. M.: State Educational Institution VUHMTs MH of the Russian Federation 2002; 608 (In Russian).





13. Paliychuk IV. The role of oral microbiocenosis and factors of local immunity in the pathogenesis of prosthetic stomatitis. *Modern dentistry* 2015; 90 (In Russian).
14. Pechinsky SV, Kuryagin AG, Oganesyanyan ET, Stepanova EF. Synthesis of lutein, Astaxanthin esters and prediction of their activity. *Journal of General Chemistry* 2019; 89(5):721-725 (In Russian).
15. Ponomareva NA, Kuryakina NV. Antibacterial properties of phyto-rinses for oral care in prosthetic carriers of elderly and senile age. *Russian Medical and Biological Bulletin of the Russian Academy of Sciences. Academician I. P. Pavlov* 2007; 4:111-116 (In Russian).
16. Shvydkaya MG, Zatevalov AM, Mitrokhin SD, Dzhandarova DT, Mironov AY. Combined effect of immunophan peptide and moxifloxacin in vitro on toxigenic strain clostridium difficile. *Clinical Laboratory Diagnostics* 2020; 65(8):516-520 (In Russian).
17. Zverev VV, Nesvizh YuV, Voropaeva EA, Afanasyev SS, Aleshkin VA, Karaulov AV, Galimzyanov KhM. Microecology and humoral immunity of human mucosal open cavities in normal and pathological conditions. Textbook for the system of postgraduate professional education of doctors. Astrakhan-Moscow: AGMA 2011; 80 (In Russian).
18. Bezrukova IV, Petrukhina, NB. Comparative assessment of various methods of using immunodon in the treatment of inflammatory periodontal diseases. *Special Issue: Stomatology-Teramedika* 2002; 10-11 (In Russian).

