

Azari Mehrdad Mohammad Ali. Periodontoprotective action of oral gel "Biotrit-Denta" in rats with sugar diabetes, received orthodontic treatment. *Journal of Education, Health and Sport*. 2018;8(8):1186-1192. eISSN 2391-8306. DOI <http://dx.doi.org/10.5281/zenodo.1451740>  
<http://ojs.ukw.edu.pl/index.php/johs/article/view/6164>

The journal has had 7 points in Ministry of Science and Higher Education parametric evaluation. Part b item 1223 (26/01/2017).  
1223 Journal of Education, Health and Sport eISSN 2391-8306 7

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The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 02.08.2018. Revised: 14.08.2018. Accepted: 31.08.2018.

UDK 616.31:616.37:616.179:379:008

## PERIODONTOPROTECTIVE ACTION OF ORAL GEL "BIOTRIT-DENTA" IN RATS WITH SUGAR DIABETES, RECEIVED ORTHODONTIC TREATMENT

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### **Abstract**

**Background.** Significant changes in diabetes mellitus are observed in the oral cavity, which can affect by treatment measures. The purpose of this study was to determine the therapeutic effect of oral phyto-gel "Biotrit-Denta" on periodontal tissues of rats with experimental diabetes mellitus and received orthodontic treatment.

**Methods.** Type 1 diabetes mellitus (DM1) was reproduced by alloxan. From 12-th day of the experiment rats were fixed in the month with orthodontic springs. One group of rats from the first day of the experiment received daily oral application gel "Biotrit-Denta". The duration of the experiments was 35 days. In the gum the level of inflammation markers (elastase, MDA), activity of urease, lysozyme, catalase were determined. The bone tissue of the alveolar process, the activity of alkaline phosphatase (ALP) and acidic phosphatase (AcP), the content of calcium and protein were determined.

Results. Diabetes mellitus causes in periodontitis of rats the development of inflammation, dysbiosis, decrease in immunity, antioxidant defense and the mineralizing activity of bone tissue. The orthodontic operation was no effect on the periodontal parameters that were changed in diabetes. Oral applications of gel "Biotrit-Denta" eliminated the phenomena of inflammation, dysbiosis and normalized the mineralising activity of bone tissue.

Conclusion. Oral applications of gel "Biotrit-Denta" have periodontoprotective effect.

**Keywords:** diabetes mellitus, paradontium, dysbiosis, inflammation, oral gel "Biotrit-Denta".

## **INTRODUCTION**

As is known, diabetes mellitus causes significant disturbances in metabolism, immune system, endoecology and in systems of organism adaptation [1-6]. Significant changes in diabetes mellitus are observed in the tissues of the oral cavity [7-10], which can affect the effectiveness of treatment measures produced in patients with diabetes mellitus.

The purpose of this study was to determine the therapeutic and prophylactic effects of the mucosa-adhesive oral phytogel "Biotrit-Dent", containing biologically active substances from wheat seedlings, lecithin, calcium citrate, NaF and ascorbic acid, on periodontal tissues of rats with experimental diabetes mellitus and received standard orthodontic treatment (installation of springs).

## **MATERIAL AND RESEARCH METHODS**

The experiments were performed on 24 white Wistar rats (males, 4 months old, initial living weight  $181 \pm 9$  g) distributed into 4 equal groups: 1st control (intact), 2nd, 3rd and 4th - Type 1 diabetes mellitus (DM1), which was reproduced once / in peritoneal administration of alloxan at a dose of 100 mg / kg [11]. Rats of the 3rd and 4th groups, starting from the 12th day of the experiment, were fixed in the mouth with orthodontic springs [12]. Rats of the 4th group from the first day of the experiment received daily oral applications of Biotrit-Denta gel at a dose of 0.5 ml / rat. The duration of the experiment was 35 days, after which the rats were sacrificed under thiopental anesthesia (20 mg / kg) by total bloodletting from the heart. The gum was excised and the alveolar process of the lower jaw was allocated.

In the gum homogenate, the level of biochemical markers of inflammation was determined [13]: elastase activity and malonic dialdehyde content, activity of the bacterial urease

[14], lysozyme activity (index of non-specific immunity level) [14] and antioxidant catalase enzyme activity [13]. The antioxidant-prooxidant index of API was calculated from the ratio of catalase activity and MDA content [13], and the degree of disbiosis according to Levitsky [14] was calculated from the ratio of relative activities of urease and lysozyme.

In the homogenate of the bone tissue of the alveolar process, the activity of alkaline (AIF) and acidic (AcF) phosphatases [15], calcium content [15] and protein [15] was determined. The mineralizing index (MI) was calculated from the ratio of AIF / AcF, and the degree of mineralisation (DM) was calculated from the ratio of calcium and protein content [16].

The results of the studies were subjected to a standard statistical treatment.

Phytogel "Biotrit-Denta" was prepared in accordance with the recipe RC U 20.4-13903778-032 / 15: 2018, using a dietary supplement with the same name (TU U 013903778-45-97) in an amount of 10% of the mass of the gel CMC-Na.

## RESULTS AND DISCUSSION

Table 1 presents the results of the determination in the gums of the rats of two markers of inflammation, elastase and MDA. From these data it is clear that in diabetes mellitus the level of elastase is significantly increased by 36.2% and MDA by 90.5%. The orthodontic operation did not significantly affect the elevated level of elastase and MDA, whereas the Biotrit-Dent gel applications completely normalized both indices, which indicates a high anti-inflammatory activity of the gel.

Table 1. Effect of Biotrit-Denta gel on the level of markers of inflammation in the gum of the rats with diabetes mellitus, who received orthodontic treatment (M ± m)

No	Groups	Elastase, $\mu$ kat/kg	MDA, mmol/kg
1	Control	27,1±1,2	9,5±0,8
2	Type 1 diabetes mellitus (DM1)	36,9±2,0 p<0,01	18,1±1,4 p<0,01
3	DM1 + orthodontic treatment (OT)	35,3±1,8 p<0,01; p <sub>1</sub> >0,3	17,4±1,2 p<0,01; p <sub>1</sub> >0,3
4	DM1 + ot+ gel «Biotrit_denta»	28,8±11,5 p>0,3; p <sub>1</sub> <0,05 p <sub>2</sub> <0,05	11,2±0,9 p>0,05; p <sub>1</sub> <0,01 p <sub>2</sub> <0,01

Notes: p - in comparison with gr. No. 1; p<sub>1</sub> - in comparison with gr. № 2; p<sub>2</sub> - in comparison with gr. No. 3.

Table 2 presents the results of determining the activity of urease, lysozyme and the degree of dysbiosis in the gingiva. It can be seen that rats with diabetes mellitus almost 2.8 times increased urease activity, which indicates a significant increase in microbial contamination of the gum. The activity of lysozyme in the gum decreases by 37.4%. Orthodontic surgery is not significantly affected on these indicators, however oral applications of the Biotrit-Dent gel significantly reduce the activity of urease and practically normalize the level of lysozyme.

Table 2. Effect of Biotrit-Denta gel on the activity of urease and lysozyme in the gum of the rats with diabetes mellitus, who received orthodontic treatment.

No	Group	Urease, $\mu$ kat/kg	Lysozyme, units/kg	Degree of dysbiosis, units
1	Control	0,51±0,09	219±27	1,0±0,2
2	Type 1 diabetes mellitus (DM1)	1,42±0,20 p<0,01	137±24 p<0,05	4,5±0,4 p<0,01
3	DM1 + orthodontic treatment (OT)	1,39±0,21 p<0,01; p <sub>1</sub> >0,5	144±21 p<0,05; p <sub>1</sub> >0,5	4,1±0,3 p<0,01; p <sub>1</sub> >0,3
4	DM1 + ot+ gel «Biotrit_denta»	0,67±0,12 p>0,1; p <sub>1</sub> <0,05 p <sub>2</sub> <0,05	207±22 p>0,3; p <sub>1</sub> <0,05 p <sub>2</sub> >0,05	1,4±0,2 p>0,2; p <sub>1</sub> <0,01 p <sub>2</sub> <0,01

In rats with diabetes, the degree of dysbiosis increases 4.5 times, but the gel applications are normalized.

Table 3 presents the results of determining the activity of catalase and the API index in the gingiva. It can be seen that in rats with diabetes the catalase activity is reliably reduced and the API index is 2.2 times higher. These indicators are also reduced to the same extent after orthodontic surgery. The application of the gel completely restores the activity of lysozyme and significantly increases the level of API.

Table 3. Effect of Biotrit-Denta gel on catalase activity and antioxidant prooxidant index (API) in the gum of the rats with diabetes mellitus, who received orthodontic treatment

No	GROUPS	Catalase, mkat/kg	API, units
1	Control	7,0±0,3	7,4±0,3
2	Type 1 diabetes mellitus (DM1)	6,0±0,3 p<0,05	3,3±0,2 p<0,01
3	DM1 + orthodontic treatment (OT)	6,6±0,4 p>0,3; p <sub>1</sub> >0,1	3,8±0,4 p<0,01; p <sub>1</sub> >0,2
4	DM1 + ot+ gel «Biotrit_denta»	7,2±0,4 p>0,3; p <sub>1</sub> <0,05; p <sub>2</sub> >0,3	6,4±0,5 p>0,05; p <sub>1</sub> <0,015 p <sub>2</sub> <0,05

Table 4 shows the results of the determination of phosphatase activity in the bone tissue. From these data it can be seen that in diabetes mellitus, the activity of alkaline phosphatase is almost halved and the activity of AcF is increased by 1.5 times, which leads to a triple reduction in the MI index. A similar change in the level of phosphatases is observed after orthodontic surgery. Gel applications completely restore the normal level of phosphatases and MI index.

Table 4. Effect of Biotrit-Dent gel on the activity of phosphatases in bone tissue the alveolar process of the lower jaw of rats with diabetes mellitus, who received orthodontic treatment

No	Group	Alkaline Phosphatase, $\mu\text{kat/kg}$	Acid Phosphatase, $\mu\text{kat/kg}$	Mineralising Index (MI), units
1	Control	102,5±6,9	8,8±0,7	11,6±0,3
2	Type 1 diabetes mellitus (DM1)	51,3±8,7 p<0,01	13,6±0,9 p<0,01	3,8±0,2 p<0,01
3	DM1 + orthodontic treatment (OT)	67,2±9,0 p<0,05; p <sub>1</sub> >0,05	11,9±1,1 p<0,05; p <sub>1</sub> >0,1	5,6±0,3 p<0,01; p <sub>1</sub> <0,05
4	DM1 + ot+ gel «Biotrit_denta»	101,8±10,2 p>0,5; p <sub>1</sub> <0,01 p <sub>2</sub> <0,05	9,1±0,8 p>0,3; p <sub>1</sub> <0,01 p <sub>2</sub> <0,05	11,2±0,4 p>0,3; p <sub>1</sub> <0,01 p <sub>2</sub> <0,01

Table 5 shows the results of the determination of protein and calcium in bone tissue. As can be seen from these data, the protein content in the bone changes little, while the calcium content significantly decreases in rats with diabetes and completely normalizes after gel applications.

Table 5. Effect of Biotrit-Dent gel on protein and calcium content in bone tissue periodontal rats with diabetes mellitus receiving orthodontic treatment ( $M \pm m$ )

No	Group	Protein, g/kg	Calcium, g/kg	The degree of mineralisation (DM)
1	Control	29,7±2,0	69,8±5,1	2,35±0,19
2	Type 1 diabetes mellitus (DM1)	25,4±1,9 p>0,05	57,2±3,0 p<0,05	2,25±0,25 p>0,3
3	DM1 + orthodontic treatment (OT)	25,1±2,0 p>0,05; p <sub>1</sub> >0,5	58,9±4,1 p>0,05; p <sub>1</sub> >0,3	2,35±0,30 p>0,5; p <sub>1</sub> >0,5
4	DM1 + ot+ gel «Biotrit_denta»	27,9±2,2 p>0,3; p <sub>1</sub> >0,3 p <sub>2</sub> >0,3	71,7±4,3 p>0,3; p <sub>1</sub> <0,05 p <sub>2</sub> <0,05	2,57±0,27 p>0,3; p <sub>1</sub> >0,3 p <sub>2</sub> >0,3

Notes: p, p<sub>1</sub> and p<sub>2</sub> - see Table 1.

The degree of bone mineralization due to large variability of the data does not change significantly.

### **CONCLUSIONS**

1. Diabetes mellitus causes in rats development in the periodontis of inflammation, dysbiosis and a decrease in the mineralising activity of bone tissue.

2. Orthodontic operation has practically no effect on the periodontal parameters that are lower in diabetes.

3. Mucozo-adhesive gel "Biotrit-Denta" has a periodontoprotective effect, eliminating the phenomena of inflammation, dysbiosis and normalizing the mineralising activity of bone tissue.

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