



## Prospects for application of polyphenolic products of grape processing in maxillofacial surgery

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### Abstract

259 maxillofacial patients with metabolic syndrome (MS) as a concomitant disease were under observation. They underwent treatment in in-patient department and entered sanatorium-resort rehabilitation. Numbers of patients with coronary heart disease (CHD) amounted to 96 patients and patients with hypertension (HD) amounted to 163, these diagnosis CHD and HD was established earlier in medical institutions. Complex therapy for patients in the main groups additionally included polyphenols in the form of red grape processing products (Enoant for 1<sup>st</sup> main group and Fenokor for 2d main group) with calculation of 10 mg of total polyphenols per 1 kg of body weight. The control group included 40 people - patients with CHD, comparable in age and sex, who received only basic sanatorium resort treatment without polyphenols application. Patients underwent biochemical and immunological examination. The decrease in the intensity of the systemic inflammatory response was confirmed by both clinical data and a significant decrease in the level of leukocytes, especially in patients with CHD. So in the group with Enoant application, the level of leukocytes decreased by 24.2% ( $p < 0.01$ ), in the group using Fenokor decreased by 29.4% ( $p < 0.01$ ). The prescription of Fenokor reduced ESR by 37% ( $p < 0.1$ ), Enoant reduced by 28% ( $p > 0.1$ ). In the study groups using grape processing products (UGPP), a decrease in the level of secondary products of lipid peroxidation (LPO) was evident on the fifth day by 30.3% ( $p < 0.001$ ), while using Fenokor, which is 10.6% and 13.4%, respectively different from the data obtained in the control group. The use of UGPP also contributed to a decrease in the level of C-reactive protein (CRP) in patients with metabolic syndrome. Thus, in the group of patients with CHD, the administration of Fenokor and Enoant led to a decrease in the level of CRP in patients by 42.7% ( $p < 0.002$ ), and in the group of patients with hypertension - by 39.9% ( $p < 0.001$ ) in comparison with the initial indicators. At the same time, a decrease in CP of blood plasma by 12.4% was observed in both main groups ( $p = 0.064$ ). This suggests that UGPP can be used in the complex treatment of maxillofacial patients, to optimize recovery processes, as well as to reduce the risk of complications caused by the influence of concomitant pathology (metabolic syndrome, HD and CHD).

**Keywords:** maxillofacial pathology, metabolic syndrome, complex postoperative treatment, grape polyphenols

### Introduction

One of the important tasks in maxillofacial surgery (MFS) continues to be the prevention of postoperative complications, as well as optimizing the conditions for the rehabilitation of patients after surgical treatment. The main cause of the development of local infectious purulent-inflammatory complications is considered to be immunodeficiency due to the presence of odontogenic foci of chronic inflammation in the area of the surgical treatment performed at the MFS with high contagious micro-flora content, which leads to the inhibition of reparation processes and regeneration of operated tissues. To compensate the effects of the prolonged negative impact of pathogenic microflora, a number of traditional

methods have been proposed, which are aimed at overcoming local infection and do not lead to immune-correction and optimization of the process of restoring injured tissues. In order to increase the effectiveness of complex treatment, the use of medications with a common antioxidant and metabolic (improving metabolic processes in damaged tissues) action is recommended. Evident antioxidant activity was revealed in preparations made from medicinal plants containing polyphenols [10]. At the same time, dentists and surgeons give priority to preparations that have a combined therapeutic effect on the patient's body, do not violate the pH of the oral fluid, and thus do not create favorable conditions for the development of dysbacteriosis.

Among the important factors affecting the course of the postoperative wound process include metabolic syndrome. Its corrective effects allow indirectly regulate the activity of local immunity. It is known that varied diversity of agricultural products, both of natural origin and low cost, continue to be a rich source of resources for the production of safe and highly effective preparations [1, 2, 3, 4, 9]. It is established that one of the richest sources of biologically active polyphenols is grapes. Content of unique combination of polyphenols (quercetin and resveratrol) makes it a promising product for the production of new nutraceuticals [7, 8].

The aim of the study was to evaluate the possibility of using polyphenolic grape processing products (Fenokor and Enoant) with antioxidant activity, optimizing metabolic processes in patients with maxillofacial pathology occurring against the background of metabolic syndrome (MS).

### Materials and Methods

The work was carried out on the basis of the state unitary enterprise of the Republic of Crimea "Ai-Petri Sanatorium". 259 maxillofacial patients who completed treatment in a hospital were under control. They underwent the sanatorium-resort rehabilitation from various regions located on the mainland of the Russian Federation. Patients were selected for the study by continuous sampling method followed by randomization, and taking into account. The criteria for the duration of the sanatorium resort treatment (at least 15 days) was considered. The informed consent of the patients for inclusion in the study was received. Total number of Patients coronary heart disease (CHD) amounted to 96, and number of patients with hypertension (HT) amounted to 163 patients. The diagnosis of CHD and HT in all patients was established earlier in medical institutions, where they received referrals for sanatorium resort treatment, and the diagnosis was confirmed upon admission to the sanatorium. The structure of the group of patients with coronary heart disease: 34 men (44.7%) and 42 women (55.3%), median age was 61.0 years (from 46.0 to 77.0 years). The structure of the group of patients with HT: 105 (73.4%) men and 38 (26.6%) women, the median age of the patients was 57.5 years (from 37.0 to 75.0 years). All patients received identical complex of basic sanatorium health treatment and necessary medications, in accordance with the approved protocols of basic therapy at the stage of sanatorium health treatment. Complex therapy was additionally included by the intake of polyphenols in the form of red grape processing products (Enoant and Fenokor preparations) with calculation of 10 mg of total polyphenols per 1 kg of body weight in the main groups of patients. The administration of polyphenols to patients was carried out definitely individually according to indications and doses. In the 1st main group, the Enoant preparation (TU 9168-001-1149102052978-14 with change 1.) was used as UGPP at a dose of 3.6 ml / kg per day, divided into two doses (lunch / dinner). "Extract of grape polyphenols," Fenokor "(TU 9168-

003-1149102052978-14) was used in the 2nd main group. The prescribed dose included 0.45 ml / kg per day, divided into two doses (lunch / dinner time).

The control group consisted of 40 people - patients with CHD (n = 20) and HD (n = 20), comparable in age and sex, who received only basic sanatorium resort treatment without the use of polyphenols. In all groups, a general blood test was made with a leukocyte count and erythrocyte sedimentation rate. The intensity of free-radical lipid oxidation in blood serum was evaluated by the concentration of the active products of thiobarbituric acid (TBA-AP). The level of TBA-AP was evaluated by the color reaction with 2-thiobarbiturate acid in the presence of Fe<sup>3+</sup>. The level of antioxidant status was determined by the concentration of ceruloplasmin of blood plasma (according to the Revin method) and the degree of tension of the acute phase response - by the concentration of C-reactive protein (immunoturbidimetric method). The results were analyzed by methods of variation statistics, using the Microsoft Excel software package. Statistical analysis was performed using the Mann-Whitney U-test; data were considered reliable at p < 0.05.

### Results

On the fifth day in the study groups using UGPP, a decrease in the level of secondary products of lipid peroxidation (LPO) was found to be reduced by 30.3% (p < 0.001) while using Enoant, and by 32.3% (p < 0.001) while using Fenokor which is 10.6% and 13.4%, respectively different from the data obtained in the control group. The use of UGPP also contributed to a decrease in the level of C-reactive protein (CRP) in patients with metabolic syndrome. Thus, in the group of patients with coronary artery disease, the administration of Fenokor and Enoant led to a decrease in the level of CRP in patients by 42.7% (p < 0.002), and in the group of patients with hypertension - by 39.9% (p < 0.001) in comparison with the initial indicators. At the same time, a decrease in CP of blood plasma by 12.4% was observed in both main groups (p = 0.064). The decrease in the intensity of the systemic inflammatory response was confirmed by both clinical data and a significant decrease in the level of leukocytes, especially in patients with coronary artery disease. So in the group using Enoant. the level of leukocytes decreased by 24.2% (p < 0.01), and in the group using Fenokor - by 29.4% (p < 0.01). In addition, a decrease in ESR in patients with coronary heart disease also indicated a decrease in the intensity of the systemic inflammatory response. So, the appointment of Fenokor reduced ESR by 37% (p < 0.05), Enoant - by 28% (p > 0.1). Moreover, in the control group, ESR decreased unreliably by 19% at (p > 0.1). Similar data were obtained in comparison groups before and after the course of treatment (Table I, Table 2).

Table 1

Index series			KPA mkM*1/sec		CP, mg/l	
			Value		Value	
			before treatment	after treatment	before treatment	after treatment
MS +CHD (n = 96)	control index n=20	M	194,52	187,56	153,68	158,79
		Σ	26,04	25,11	22,38	29,53
	1-st main (Enoant) n=39	M	136,97	154,97	199,07	143,49
		Σ	24,82	20,09	21,89	23,59
	2-nd main (Fenokor) n=37	M	185,15	230,91	181,91	139,97
			31,23	26,06	30,54	24,40
MS +HD (n= 163 )	control index n=20	M	178,00	163,07	169,74	149,26
		Σ	28,21	22,55	28,12	22,65
	1-st main (Enoant) n=72	M	177,17	198,35	175,38	141,26
		Σ	27,03	21,37	35,03	23,19
	2-nd main (Fenokor) n=71	M	154,00	207,18	191,42	148,10
		Σ	26,79	22,16	35,88	26,48

Table 2

Index series			TBA -AP, nM*MDA/ml		Diene conjugates unit/ml	
			Value		Value	
			before treatment	after treatment	before treatment	after treatment
MS +CHD (n = 96)	control index n=20	M	194.52	137,56	3,17	2.94σ
		σ	26,04	25,11	0,32	0,28
	1-st main (Enoant) n=39	M	186,97	134,97	3,02	2,18
		σ	34,82	20,09	0,30	0,27
	2-nd main (Fenokor) n=37	M	185,15	130,91	2,95	2,21
			31,23	26,06	0,28	0,23
MS +HD (n= 163 )	control index n=20	M	178.00	163,07	2.87	2.65
		σ	28,21	32,55	0,27	0,25
	1-st main (Enoant) n=72	M	177.17	168,35	2,95	2,24
		σ	27,03	21,37	0,28	0,22
	2-nd main (Fenokor) n=71	M	184,00	177,18	3,07	2,45
		σ	26,79	22,16	0,29	0,27

**Notes:** quantitative values are presented in the format:  $M \pm \sigma$ , Me (Q<sub>25%</sub>; Q<sub>75%</sub>). Accuracy of differences at (p < 0.05): \* - between the main and control groups,

## Discussion

Data submitted in Table I and 2 give grounds to believe that the preparation "Fenokor" exhibits significantly more pronounced antioxidant activity than "Enoant". The ratio of antioxidant activity with mass concentration, which is 5 times higher for Fenokor (200 to 80 g / dm<sup>3</sup>) than Enoant (40 to 22 g / dm<sup>3</sup>)<sup>[11, 5]</sup> is a possible explanation of this phenomenon. Considering the evident effect of the "Fenokor" preparation on the course of the metabolic syndrome, manifested in decrease in the levels of LPO, CRP and blood plasma CP and decrease in the intensity of the systemic inflammatory reaction, confirmed by the data of both clinical studies and a significant decrease in the level of white blood cells, it should be considered that "Fenokor" makes a considerable effect on the course of inflammatory processes in the body as a whole, as it has a vivid general immunocorrection effect on the body of patients with MS with concomitant pathology in the form of coronary heart disease or HD<sup>[6]</sup>.

## Conclusion

The use of grape polyphenols in the conditions of sanatorium-resort rehabilitation of maxillofacial patients with concomitant CHD and HD developed against the background of the metabolic syndrome showed a high activity of these products against pro-inflammatory markers and free radical damage to

body tissues.

Grape derivatives with a high concentration of polyphenols (80 g / dm<sup>3</sup>) show evident antioxidant and anti-inflammatory effects that can be used in the complex treatment of maxillofacial patients to optimize recovery processes, as well as to reduce the risk of complications due to the influence of concomitant pathology (metabolic syndrome HD and CHD). UGPPs can be used most effectively in the complex treatment of patients with infectious purulent inflammatory diseases in the maxillofacial operations due to their immune-corrective effect on the body. Conflict of interest. The authors declare no conflict of interests.

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