



## The efficiency of the use of polyphenolic grape processing products in the treatment of experimental metabolic syndrome

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### Abstract

For 12 weeks, grape polyphenols were used in 30 Wistar rats on the background of a fructose model of metabolic syndrome. All the animals were on a standard food diet. 3 groups of observations were formed: the 1st "control" (10 animals received 100 ml of 2.5% fructose solution daily); the 2nd "experimental" (10 rats were given the drug "Fanokor" with a total content of polyphenols of 181.53 g/dm<sup>3</sup>, at the rate of 10-15 ml per 1 animal per day in addition to fructose solution); the 3rd "experimental" (10 animals together with a solution of fructose were given the drug "Enoant" with a total content of polyphenols of 4.20 g/dm<sup>3</sup>, at the rate of 10-15 ml per 1 animal per day). Animals were measured weekly abdominal circumference and body weight. At the end of the experiment, the morphological structure of the liver, kidneys and abdominal fat was studied in all representatives of the comparison groups. The results were analyzed using the methods of variational statistics and Microsoft Excel software. The statistical analysis was carried out using the Mann-Whitney U-test; the data were considered reliable at  $p \leq 0.05$ . Microscopic examination of abdominal fat revealed mild and moderate residual diffuse lymphoplasmocytic infiltration in addition to edema, fullness and single petechial hemorrhages. Focal dystrophic changes of hepatocytes were determined, in combination with weakly expressed, mainly periportal, less often diffuse intralobular lymphohistiocytic infiltration and with signs of hemodynamic disorders. The signs of blood circulatory disorders, primarily the fullness of the capillary loops of the glomeruli and single weakly expressed lymphoid clusters in the interstitial, mainly perivascular and in the paranephral tissue stand out during microscopy of the kidney tissues of rats who underwent correction of the metabolic syndrome by "Enoant".

The analysis of the obtained results allows us to conclude that the use of grape polyphenols in the composition of "Fanokor" inhibits the development of negative structural and morphofunctional changes in the tissues of the heart, liver, kidneys and visceral cellular in the conditions of modeling the metabolic syndrome, and also optimizes the regeneration in these organs. The obtained data give grounds to recommend polyphenolic products of grape processing for inclusion in the complex of treatment of maxillofacial patients with infectious odontogenic inflammatory diseases developed on the base of metabolic syndrome.

**Keywords:** experimental metabolic syndrome, treatment, grape polyphenols, morphological study

### Introduction

Improving the effectiveness of surgical treatment of patients with background pathology continues to be a relevant direction in medicine. The number of patients with two or more diagnoses of chronic diseases has continued its steady growth in recent years. A special direction is the metabolic syndrome, accompanied by an increase in body weight, the development of diabetes mellitus and cardiovascular diseases (such as coronary heart disease and hypertension), a decrease in the activity of reparative processes, as well as an increased load on the human immune system [1, 2, 3].

The frequency of intra - and postoperative complications in such patients (hypertension, bleeding, PATE, hematomas, disorders of regeneration processes) remains high even with the use of modern methods of drug prevention and postoperative care [4].

To prevent the development of these complications and optimize the healing process of a postoperative wound, complex treatment is enhanced with means having antioxidant and metabolic effects, having a pH that contributes to the creation of conditions that are not suitable for the vital activity of pathogenic microorganisms. The group of such drugs

includes polyphenolic products of grape processing (Fenocor and Enoant) <sup>[5, 6]</sup>.

Thus, the aim of the study was to evaluate the therapeutic effectiveness of polyphenolic grape processing products (using the example of the drugs "Fanokor" and "Enoant") and the prospects for their use in maxillofacial surgery in an experimental model of metabolic syndrome.

### Materials and methods

30 Wistar rats were monitored for 12 weeks. All animals used a standard food ration. In addition to it, the animals received: in the 1st (control) group (10 animals) 100 ml of 2.5% fructose solution daily; in the 2nd (experimental) group (10 animals), the drug "Fanokor" with a total content of polyphenols of 181.53 g/dm<sup>3</sup> was given daily together with a fructose solution, at the rate of 10-15 ml per 1 animal per day. Representatives of the 3rd (experimental) group (10 animals) received together with a solution of fructose the drug "Enoant" with a total content of polyphenols of 4.20 g/dm<sup>3</sup>, at the rate of 10-15 ml per day.

During the experiment, the animals were measured weekly abdominal circumference and body weight. At the end of the experiment (12 weeks), the rats were removed from the experiment by decapitation under ether anesthesia.

The results were analyzed using the methods of variational statistics, using the Microsoft Excel computer software package. The statistical analysis was carried out using the Mann-Whitney U-test; the data were considered reliable at  $p < 0.05$ .

### Results

In the experiment, in animals with a simulated metabolic syndrome who took the drug "Fanokor" (group 2), body weight and abdominal circumference after 12 weeks significantly differed from the control figures of the representatives of the first group ( $p < 0.05$ ). A pathohistological examination of abdominal fat revealed weakly expressed lymphoplasmocytic infiltration in presence of hemodynamic disorders in the form of edema, fullness of blood and single petechial hemorrhages (Fig.1). It should also be noted that in this group, adipocytes had variable sizes (Fig. 2).

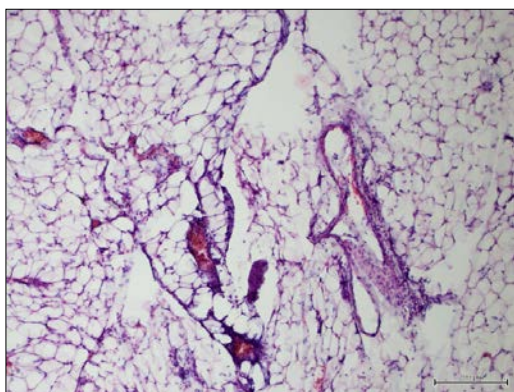


Fig 1

Focal dystrophic changes of hepatocytes were also detected in micro-preparations of the same group (with the use of the Fenokor), in combination with weakly expressed mainly

periportal, less often diffuse intralobular lymphohistiocytic infiltration and residual signs of hemodynamic disorders (Fig. 2).

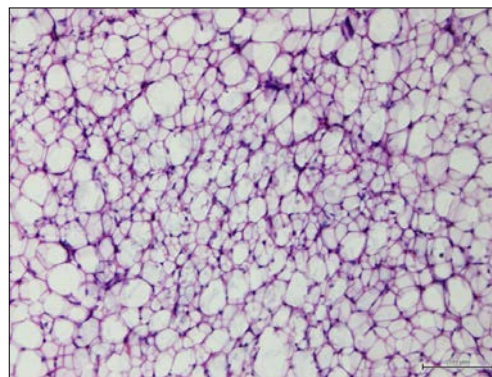


Fig 2

Microscopic examination of the kidney tissues of rats who underwent correction of the metabolic syndrome with the drug "Enoant" (group 3) revealed a morphological picture close to that observed with the use of the drug "Fanokor" (group 2). However, signs of blood circulatory disorders attracted attention, primarily the fullness of the capillary loops of the glomeruli and single weakly expressed lymphoid clusters in the interstitium, mainly perivascular and in the paranephral tissue (Fig. 4).

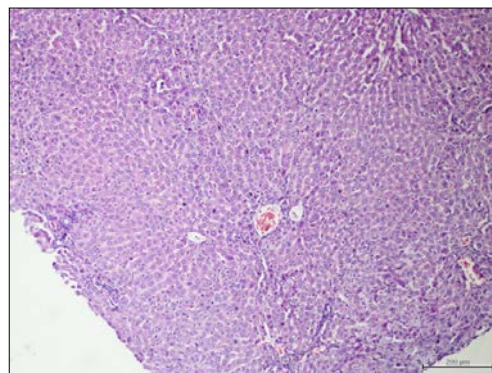


Fig 3

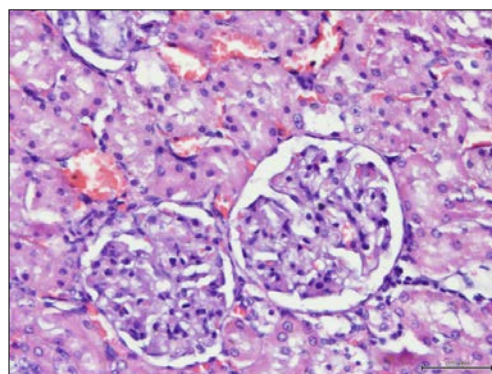
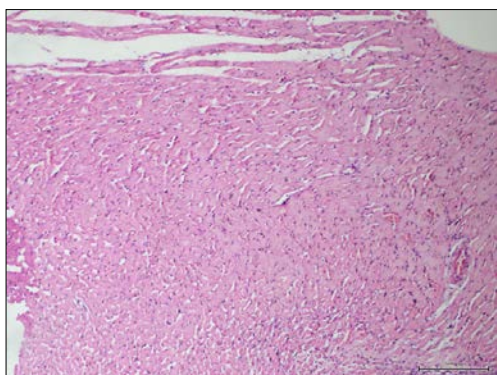


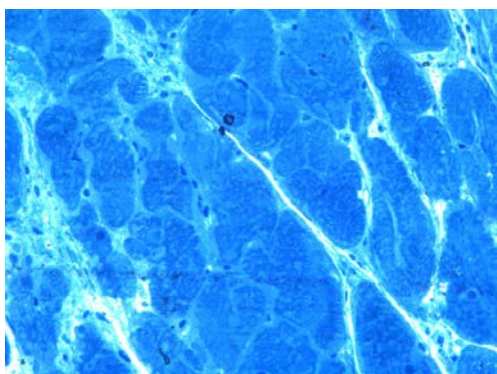
Fig 4

In the myocardium, morphological changes were the least in the representatives of the 2nd (experimental) group (with the

use of the drug Fenokor), muscle fibers here had a typical structure and adipocytes between them were found only focally, closer to the epicardium, but in the myocardium there were still phenomena of edema and vascular fullness (Fig. 5 and 6)

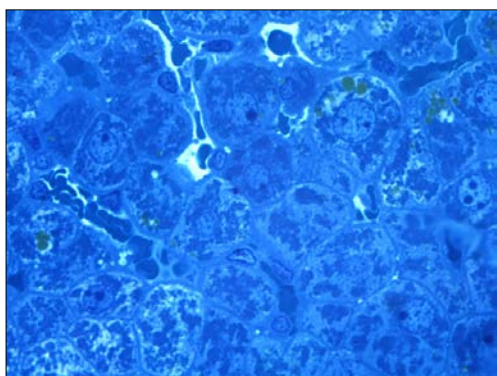


**Fig 5**



**Fig 6**

The most striking pathomorphological changes were detected in representatives of the 1st (control) group. So, in the liver tissue, part of the sinusoid capillaries was expanded and filled with red blood cells. Here, the stasis and sludge of erythrocytes in the form of coin columns were also noted. Along with the expanded hemocapillaries, narrowed hemocapillaries were found, which is due to hypertrophy of hepatocytes and endotheliocytes. The morphology of the microcirculatory blood flow system as a whole indicated a violation of intra-lobular hemodynamics (Fig. 7).



**Fig 7**

## Discussion

The given data gives reason to believe that the drug "Fanokor" shows a more pronounced therapeutic activity than "Enoant". The probable reason for this is the unequal ratio of the mass concentration of polyphenols in the preparations, which is 5 times higher in Fanokor (200 to 80 g/dm<sup>3</sup>) than in Enoant (40 to 22 g/dm<sup>3</sup>) [7, 8, 9].

Thus, the pronounced effect of the drug "Fanokor", in the treatment of metabolic syndrome in experimental animals, came out in the study of such markers as normalization of body weight, rapid extinction of signs of lymphoplasmocytic infiltration, edema and hemodynamic disorders in the abdominal region. The data obtained during the study indirectly confirm that Fanokor has a pronounced general immunocorregulating effect on the body of animals with expanded MS and can be successfully used in the complex treatment of this disease. Due to the fact that MS is one of the leading factors contributing to the development of intra- and postoperative complications, its use of Fanokor can contribute to improving the effectiveness of complex treatment of maxillofacial surgical patients [10, 11, 12].

## Conclusion

The use of grape polyphenols in laboratory rats with artificially modeled metabolic syndrome showed a high activity of these products in relation to the prevention of the development of negative structural and morpho functional changes in the tissues of the heart, liver, kidneys and visceral tissue in the studied pathological condition.

Grape derivatives with a high concentration of polyphenols (80 g/dm<sup>3</sup>) due to pronounced antioxidant and anti-inflammatory effects, optimize regenerative processes in affected tissues and organs, which reduces the risk of complications due to local trophic disorders, including due to the negative impact of concomitant pathology (metabolic syndrome). The obtained data on the effectiveness of grape polyphenol processing products can be used in the clinic in the treatment of patients with infectious purulent odontogenic inflammatory diseases in the maxillofacial region in the setting of metabolic syndrome.

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