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NAS RK is pleased to announce that Bulletin of NAS RK scientific journal has been accepted for indexing in the Emerging Sources Citation Index, a new edition of Web of Science. Content in this index is under consideration by Clarivate Analytics to be accepted in the Science Citation Index Expanded, the Social Sciences Citation Index, and the Arts & Humanities Citation Index. The quality and depth of content Web of Science offers to researchers, authors, publishers, and institutions sets it apart from other research databases. The inclusion of Bulletin of NAS RK in the Emerging Sources Citation Index demonstrates our dedication to providing the most relevant and influential multidiscipline content to our community.

Қазақстан Республикасы Ұлттық ғылым академиясы "ҚР ҰҒА Хабаршысы" ғылыми журналының Web of Science-тің жаңаланған нұсқасы Emerging Sources Citation Index-те индекстелуге қабылданғанын хабарлайды. Бұл индекстелу барысында Clarivate Analytics компаниясы журналды одан әрі the Science Citation Index Expanded, the Social Sciences Citation Index және the Arts & Humanities Citation Index-ке қабылдау мәселесін қарастыруда. Web of Science зерттеушілер, авторлар, баспашылар мен мекемелерге контент тереңдігі мен сапасын ұсынады. ҚР ҰҒА Хабаршысының Emerging Sources Citation Index-ке енуі біздің қоғамдастық үшін ең өзекті және беделді мультидисциплинарлы контентке адалдығымызды білдіреді.

НАН РК сообщает, что научный журнал «Вестник НАН РК» был принят для индексирования в Emerging Sources Citation Index, обновленной версии Web of Science. Содержание в этом индексировании находится в стадии рассмотрения компанией Clarivate Analytics для дальнейшего принятия журнала в the Science Citation Index Expanded, the Social Sciences Citation Index и the Arts & Humanities Citation Index. Web of Science предлагает качество и глубину контента для исследователей, авторов, издателей и учреждений. Включение Вестника НАН РК в Emerging Sources Citation Index демонстрирует нашу приверженность к наиболее актуальному и влиятельному мультидисциплинарному контенту для нашего сообщества.

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EFFICIENCY OF GRAPE POLYPHENOLS IN PATIENTS WITH METABOLIC SYNDROME (LITERATURE REVIEW)

Abstract. Purpose of the review: to study of the efficiency of grape polyphenols in patients with metabolic syndrome.

Methodology: A literature search was conducted in electronic databases and publications included in Embase, PubMed/Medline, Science Direct, Springer Link, Cochrane Library, eLibrary. The depth of the literature search was 12 years. More than 30 publications were selected and reviewed, including full-text articles, Systematic Reviews and Meta-Analysis that were published in English.

Results and conclusions: Grape polyphenols in supported doses can delay or prevent the onset of metabolic syndrome with reducing body weight, blood pressure and blood glucose levels and improving lipid metabolism. The results indicate that polyphenols are significant metabolic modulators because of their ability to influence different targets of the cellular and molecular pathways. However, some studies have shown inconsistent results and conflicting data on the efficacy of polyphenols in metabolic syndrome management have been obtained. Perhaps, contradictory data are associated with significant limitations of their bioavailability, especially in conditions of progressive metabolic syndrome. Therefore, more extensive and in-depth scientific research are needed to determine more accurately the role of polyphenols in the progression of metabolic syndrome components.

Keywords: grape polyphenols, metabolic syndrome.

Introduction. Cardiovascular disease and diabetes mellitus are currently the leading cause of death. The prevention of these diseases is an important problem and it is based on confronting risk factors. In medical practice at the stage of metabolic syndrome (MS), early detection and elimination of risk factors for cardiovascular disease and diabetes mellitus is possible. MS is a cluster of metabolic disorders that includes insulin resistance, hypertension, dyslipidemia and abdominal obesity. The prevalence of MS varies from 10% to 84% depending on the ethnicity, age, and sex [1], which makes it an important social and economic problem worldwide.

Metabolic Syndrome. International organizations and expert groups, such as the World Health Organization, the European Group for the Study of Insulin Resistance, the International Diabetes Federation, have attempted to integrate MS parameters. Nevertheless, the definition of the consensus of the International Diabetes Federation seems to be most suitable for practical use in clinical medicine, taking into account the inclusion of threshold values for different ethnic groups [3, 4]. According to this definition, MS is a cluster of the most dangerous risk factors for cardiovascular disease: central (abdominal) obesity, increased fasting plasma glucose, diabetes, high cholesterol and high blood pressure [2].

As the MS progresses, the subcutaneous abdominal adipocytes merge their lipolytic products (free fatty acids) directly into the portal vein, thereby increasing the concentration of fatty acids in the blood serum, increasing the absorption of fatty acids by the liver, skeletal muscles and beta cells of the pancreas and reducing glucose consumption. Reducing glucose consumption increases serum glucose levels and stimulates increased insulin secretion for glucose utilization: a lack of response to an additional secreted

insulin induces glucose resistance. The constantly high secretion of insulin, in turn, causes metabolic stress in the mitochondria of beta cells of the pancreas, causing the release of reactive oxygen species that damage the mitochondria and among other causes trigger the process of chronic systemic inflammation with time mitochondria lose their ability to support cellular processes, and beta- cells undergo apoptosis, irreversibly reducing the secretion of insulin. To reduce the increase in oxidative stress and inflammatory reaction means to control the onset of irreversible changes in the human body that contribute to premature aging.

Grape Polyphenols. Obviously, abdominal obesity, high blood pressure, impaired glucose tolerance, dyslipidemia and increased oxidative stress and inflammation are the interacting factors of the metabolic syndrome that can be effectively modified with dietary interventions involving polyphenol-rich foods or beverages [5]. Clinical researchers are increasingly attracted by natural healing factors in MS and one of the promising factors are grape polyphenols [6].

Polyphenols are a part of the group of antioxidants of natural origin and are plant pigments contained in large quantities in grapes and other fruits and vegetables. In addition, complexes of plant polyphenol compounds become one of the most important food additives of recent decades. Among plant polyphenols, the greatest attention is given to the research of red grape polyphenols.

Purpose of the Review. To review human studies of the effects of grape polyphenols intake in patients with MS.

Methodology of the Review. A literature search was conducted in electronic databases and publications included in Embase, PubMed/Medline, Science Direct, Springer Link, Cochrane Library, eLibrary. The depth of the literature search was 12 years (2005–2017). The following search terms were used (including synonyms and closely related words): “metabolic syndrome”, “grape polyphenols”, “effects of grape polyphenols”, “grape polyphenols”, “effect on the metabolic syndrome”, “hypertension” or “blood pressure”, “lipids” or “cholesterol”, “insulin” or “glucose”. More than 30 publications were selected and reviewed, including full-text articles, Systematic Reviews and Meta-Analysis that were published in English. They involved a clinical trial in healthy adults or adults suffering from the MS or closely related diseases such as obesity, coronary artery disease or type 2 diabetes.

Effects of Grape Polyphenols on Metabolic Syndrome. As is known, the evolution of MS passes in two directions: the development of dysfunction of β-cells of the pancreas and hyperinsulinemia with compensatory insulin resistance. Given that pro-oxidant status and chronic systemic inflammation accompany MS and that its severity, grape polyphenols manifest themselves as good dietary drugs to prevent the progression of MS by using certain mechanisms of action [7]. By modifying the inflammatory response and reducing the levels of free radicals, grape polyphenols reduce the severity of the chronic systemic inflammatory process. The mechanisms of action include both the manifestation of the antioxidant properties of polyphenols or the enhancement of the expression of antioxidant genes and proteins, as well as a decrease in the intensity of stress signals of the endoplasmic reticulum [8, 9].

According to the studies, oxidative stress occurs with systemic inflammation, endothelial dysfunction, impaired secretion of pancreatic cells and utilization of glucose in peripheral tissues, which lead to long-term secondary complications [10]. Many data from epidemiological studies indicate a positive relationship between a decrease in metabolic disorders and consumption of a diet rich in polyphenols [11].

Since polyphenols increase the antioxidant capacity of plasma, the reversibility of metabolic disorders can be explained by the adoption of an electron from active oxygen species and the formation of relatively stable phenoxy radicals. Active forms of oxygen are considered toxic by-products and pose a threat to cells, causing lipid peroxidation, protein oxidation and nucleic acid damage, inhibition of the enzyme, and activation of programmed cell death [12]. Polyphenols protect the cell constituents from oxidative damage and limit the risk of various degenerative diseases associated with oxidative stress.

Effects of Grape Polyphenols Intake in Patients with Metabolic Syndrome. At the present time, there are a number of clinical studies that are showed efficacy and safety of grape polyphenols intake in patients with MS, cardiovascular diseases, and diabetes mellitus. They indicate that polyphenols improve insulin resistance [13], reduce blood pressure [14], and body weight [15], and improve lipid metabolism [16]. However, results of other clinical studies show differential effects of grape polyphenols on MS components, and it depends on the number of MS components in every patient. However, dietary strategies may be less effective for patients with a group of MS risk factors in general than for patients with

one or two risk factors. The effects of polyphenols intake on healthy volunteers or patients with a low risk of cardiovascular disease may differ from those in patients with MS. Thus, the results of such clinical studies may be incompatible and the metabolic benefits of polyphenols intake may strongly depend on the studied population.

A systematic review [17] of the effects of grape polyphenols on the components of MS show the difference in the effects on the components of the MS. Also, in this review there is no convincing evidence that grape polyphenols can positively influence the level of glycemia, blood pressure and lipids in patients with MS.

A recent review [18] indicates that polyphenols are effective in reducing some MS components, but there is no a single extract or polyphenol that can affect all components of MS. The protective functions of polyphenols can be effective only through frequent and prolonged consumption in the long term, in the context of a healthy diet.

A review of the effects of polyphenol intake in patients with MS showed the results of the human interventional trials with polyphenols as polyphenol-rich foods and dietary patterns rich in polyphenols [19]. Evidences of this review suggest that polyphenols in supported doses may delay or prevent the onset and progression of MS by decreasing body weight, blood pressure, blood glucose and by increasing lipid metabolism. Polyphenols entering the human body, they control and normalize the metabolic processes at the cellular level, and also absorb and neutralize free radicals and stop chain reactions. In addition, in this review, many epidemiological and interventional trials have shown inconsistent results, only a small number of interventional trials indicate the benefits of polyphenol intake in improving the phenotype of MS. Long-term studies are justified in order to assess the possible preventive effects of a higher intake of polyphenols by combining their diverse dietary sources [20, 21].

Regarding the effect of polyphenols on the components of MS, some studies have shown that grape polyphenols have a potential effect on lipid metabolism and weight loss. The results of a study [22] on the effect of polyphenols on lipid metabolism in patients with type 2 diabetes on a background of overweight confirm that grape polyphenols improve lipid metabolism, reducing the plasma concentration of total cholesterol, low density lipoproteins and increasing the concentration of high-density lipoproteins.

A recent systematic review noted that weight loss caused by polyphenols is not clinically significant in people who are overweight and obese [23]. It has been indicated that many interventional trials have a duration of less than 3 months. Therefore, long-term randomized interventional trials with a duration of 12 months or more are needed to understand the effect of an intervention on weight loss and obesity prevention.

In recent years, a significant number of randomized trials have been conducted to evaluate preventive measures for type 2 diabetes and results from one of these studies [24] show the protective effects of grape polyphenols on oxidative stress and insulin resistance.

Regarding the effect of dietary polyphenolic compounds, in vitro and in vivo studies suggest improvement of glucose homeostasis through potential multiple mechanisms of action in the intestine, liver, muscle adipocytes and pancreatic β-cells, and through prebiotic effects in the digestive tract. In general, most epidemiological studies show that dietary polyphenols are associated with a lower risk of developing type 2 diabetes.

If the results of some clinical studies on the efficacy of polyphenols showed a significant reduction in hypertension [25-27], then in the other studies there were no significant changes [28, 29]. A meta-analysis [30] showed that daily consumption of grape polyphenols could significantly reduce systolic blood pressure. A significant decrease in blood pressure was noted when taking a low dose of grape polyphenols (<733 mg/day). However, results of this study indicated that diastolic blood pressure was not significantly reduced in patients in the study group as compared to controls, and therefore, this study confirms the hypothesis that daily consumption of grape polyphenols can affect systolic blood pressure, but not diastolic blood pressure.

Conclusion. Current clinical studies suggest that grape polyphenols in supported doses can delay or prevent the onset of MS, reducing body weight, blood pressure and blood glucose levels and improving lipid metabolism. Their results indicate that polyphenols are significant metabolic modulators because of their ability to influence various targets of the cellular and molecular pathways that have been proven as potential targets for the polyphenolic group of compounds.

However, some epidemiological and interventional studies have shown inconsistent results. Thus, based on the conducted review of clinical studies, conflicting data on the effects of grape polyphenols in MS patients were obtained. Perhaps, among other reasons, their inconsistency is associated with significant limitations of their bioavailability, especially in conditions of progressive MS. Therefore, more extensive and in-depth scientific studies are needed to determine more accurately the role of grape polyphenols in the progression of MS components, as well as to determine the best dose, ideal food matrix and method of administration. In this case, it is very likely to obtain an effective product for reducing the risk of cardiovascular disease in humans and prolonging active longevity.

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МЕТАБОЛИКАЛЫҚ СИНДРОМЫ БАР ПАЦИЕНТТЕРДЕ ЖҮЗІМ ПОЛИФЕНОЛЫНЫҢ ТИІМДІЛІГІ (ӘДЕБИЕТТЕРДІ ШОЛУ)

Аннотация. Мақсаты: Метаболикалық синдромы бар пациенттерде жүзім полифенолының тиімділігін зерттеу.

Әдістеме: Embase, PubMed/Medline, Science Direct, Springer Link, Кокран кітапханасы, eLibrary кіретін жарияланымдарда және электрондық дерекқорларында әдебиеттерді іздеу жүргізілді. Әдебиеттерді іздеу тереңдігі 12 жыл болды. 30-дан астам жарияланымдар қарастырылды, соның ішінде ағылшын тіліндегі толық мәтінді мақалалар, жүйелі шолулар мен мета-анализдер таңдап алынды.

Нәтижелер мен қорытындылар: Қолданылатын дозаларда жүзім полифенолы дене салмағын, қан қысымын және қан глюкозасының деңгейін төмендетумен және липидті метаболизмді жақсартумен метаболикалық синдромның басталуын болдырмайды немесе алдын алады. Нәтижелер полифенолдардың жасушалық және молекулалық жолдардың әртүрлі нысаналарына ықпал ету қабілетіне байланысты маңызды метаболикалық модулятор болып табылатынын көрсетеді. Алайда, кейбір зерттеулер метаболикалық синдромды емдеуде полифенолдардың тиімділігі туралы келісілмеген нәтижелерді және қайшы деректерді көрсетті. Мүмкін, қарама-қайшы деректер биожетімділіктің елеулі шектеулерімен байланысты, әсіресе прогрессивті метаболикалық синдром жағдайында. Сондықтан метаболикалық синдромы компененттерінің прогрессиясында полифенолдардың рөлін дәлірек анықтау үшін неғұрлым кең және терең ғылыми зерттеулер қажет.

Түйін сөздер: жүзім полифенолдары, метаболикалық синдром.

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ЭФФЕКТИВНОСТЬ ПОЛИФЕНОЛОВ ВИНОГРАДА У ПАЦИЕНТОВ С МЕТАБОЛИЧЕСКИМ СИНДРОМОМ (ОБЗОР ЛИТЕРАТУРЫ)

Аннотация. Цель обзора: Изучение эффективности полифенолов винограда у пациентов с метаболическим синдромом.

Методология: Проведен поиск литературы в электронных базах данных и публикациях, вошедших в Embase, PubMed/Medline, Science Direct, Springer Link, Кокрановскую библиотеку, eLibrary. Глубина поиска литературы составляла 12 лет. Были выбраны и рассмотрены более 30 публикации, в том числе полнотекстовые статьи, систематические обзоры и мета-анализы на английском языке.

Результаты и выводы: Полифенолы винограда в поддерживаемых дозах могут задерживать или предотвращать начало метаболического синдрома, уменьшая массу тела, артериального давления и уровень глюкозы в крови и улучшая обмен липидов. Результаты указывают, что полифенолы являются значительными метаболическими модуляторами в силу их способности влиять на различные мишени клеточного и молекулярного пути. Однако некоторые исследования показали непоследовательные результаты и получены противоречивые данные об эффективности полифенолов в управлении метаболического синдрома. Возможно, противоречивые данные связаны с существенными ограничениями их биодоступности, особенно в условиях прогрессирующего метаболического синдрома. Поэтому необходимы более объемные и глубокие научные исследования, чтобы установить более точно роль полифенолов в прогрессии компонентов метаболического синдрома.

Ключевые слова: полифенолы винограда, метаболический синдром.

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