Biol. Stud. 2023; 17(1): 35–48 • DOI: https://doi.org/10.30970/sbi.1701.704
www.http://publications.lnu.edu.ua/journals/index.php/biology

UDC: 616.379-008.64:[615.322:582.781]

THE EFFECT OF EXTRACTS OF FRUITS OF DIFFERENT CULTIVARS OF *CORNUS MAS* L. ON PLASMA LIPID PROFILE IN EXPERIMENTAL DIABETES MELLITUS

I. V. Brodyak [1], ***M. O. Chaban*** [1], ***A. A. Moroz*** [1], ***A. Z. Kucharska*** [2], ***N. O. Sybirna*** [1]

[1] *Ivan Franko National University of Lviv, 4 Hrushevsky St., Lviv 79005, Ukraine*

[2] *Wrocław University of Environmental and Life Sciences 37/41 J. Chełmoński St., 51-630 Wrocław, Poland*

Brodyak, I. V., Chaban, M. O., Moroz, A. A., Kucharska, A. Z., & Sybirna, N. O. (2023). The effect of extracts of fruits of different cultivars of *Cornus mas* L. on plasma lipid profile in experimental diabetes mellitus. *Studia Biologica*, 17(1): 35–48. doi:10.30970/sbi.1701.704

Background. Diabetes mellitus with impaired transport of glucose from the blood into the cells against the background of absolute or relative hypoinsulinemia is accompanied by the development of dyslipidemia. Therefore, it is important to find therapeutic agents capable of alleviating the symptoms and, as a result, the course of diabetes. Screening of antidiabetic agents indicates that one of their main potential sources is natural products of plant origin. However, although a wide range of plant extracts are known to be used to treat diabetes, the use of only some of them has been scientifically proven. The aim of the study was to investigate the influence of biologically active substances available in the extracts of fruits of different cultivars of *Cornus mas* L. on plasma lipid profile in experimental diabetes mellitus.

Materials and methods. Wistar male rats with starting weight of 140–170 g were used for all experiments. Diabetes was induced by intraperitoneal injection of streptozotocin (55 mg/kg of body weight). The animals were divided into five groups. The first (control) and the second (diabetic control) groups orally received 1 mL of water daily for 14 days. Diabetic animals of the third to fifth groups were orally administered extracts of red and yellow fruits of *Cornus mas* L. and the “Loganic acid” extract, respectively, in the amount of 20 mg/kg of body weight for 14 days. The concentration of low-density lipoproteins, high-density lipoproteins, triglycerides, and cholesterol was determined in the rats’ blood plasma. Atherogenic indices were calculated based on lipid profile in blood plasma.

Results. The total cholesterol content in diabetic rats' blood plasma was reliably reduced when the extract of the red fruits of the *Cornus mas* L. "Podolski" cultivar was administered. "Loganic acid" extract, obtained from the yellow fruits of the "Yantarnyi" and "Flava" cultivars of *Cornus mas L.*, decreased the concentration of total cholesterol, triglycerides, and the content of low-density lipoproteins against the background of an increase in the content of high-density lipoproteins in blood plasma. The atherogenic indexes made it possible to establish that the degree of risk of cardiovascular complications due to diabetes is significantly reduced against the background of the administration of extracts of cornelian cherry fruits.

Conclusions. Extracts of the fruits of the "Podolski", "Yantarnyi" and "Flava" cultivars of *Cornus mas* L. correct the lipid profile of blood plasma in streptozotocin-induced diabetes animals and, as a result, may potentially prevent the development of atherosclerotic changes and cardiovascular complications. The fruits of *Cornus mas* L. may be potential agents in the therapy of dyslipidemia in diabetes.

Keywords: diabetes mellitus, low-density lipoproteins (LDL), high-density lipoproteins (HDL), triglycerides (TG), total cholesterol (Total CHOL), dyslipidemia, extracts of cornelian cherry fruits (*Cornus mas* L.)

INTRODUCTION

Diabetes mellitus (DM) is the most common metabolic disorder that affects the quality of life and people's working capacity worldwide, and also increases the burden on the global healthcare system and the economy of each individual state. Not only is it important to study the pathological processes that cause the development of diabetes (Kuchurka *et al*., 2022), but also those that progress during the long-term course of this disease. The study of such mechanisms makes it possible to alleviate the condition of patients and select effective methods of correction of significantly disturbed metabolism (Dzydzan *et al*., 2022; Zhang *et al*., 2020).

This disease is associated not only with the carbohydrate and protein metabolism disorders, but also with dyslipidemia – a change in the lipid profile of blood plasma. Serological markers of dyslipidemia are changes in the content of triacylglycerols, total cholesterol and cholesterol of high-density lipoprotein (HDL-C) and low-density lipoprotein (LDL-C) in blood plasma. One of the main reasons for the development of dyslipidemia is a disturbance of the transport of glucose from the blood into cells, especially in insulin-dependent tissues. This leads to the development of an intracellular energy crisis. To reduce energy hunger in the body, compensatory mechanisms are activated: polyphagia occurs and the formation of endogenous glucose increases through gluconeogenesis – the formation of glucose from intermediate products of the catabolic breakdown of proteins and fats. The breakdown of proteins is accompanied by the depletion of the body's protein reserves against the background of the formation of increasingly larger amounts of free fatty acids in adipose tissue. Such disorders lead to structural and functional changes of cells, particularly in the intima of vessels, blood cells, and provoke complications at the level of multiple body systems – cardiovascular, excretory, and others (Zhang *et al*., 2020).

Therefore, it is important to find therapeutic agents capable of alleviating the symptoms and, consequently, the course of DM. The positive effect on diabetic conditions of

biologically active substances, particularly antioxidants included in plant extracts has been proven. Bioactive compounds exhibit a wide range of properties: hypoglycemic, anti-inflammatory, immunomodulatory, and antiatherogenic effects (Dzydzan *et al*., 2020; Seniv *et al*., 2021).

In recent years, extracts of the fruits of *Cornus mas* L. have elicited great interest due to the presence of various bioactive compounds in them and their beneficial properties. The main substances that show high biological activity in the fruits of *Cornus mas* L. are vitamin C, anthocyanins, flavonoids and iridoids (Efenberger-Szmechtyk *et al.*, 2020). The fruits of the cornelian cherry, depending on the variety, differ in the qualitative and quantitative composition of biologically active substances (Dzydzan *et al*., 2019, 2020). It should be noted that various cultivars of *Cornus mas* L. are common in Ukraine and Central Europe. The "Podolski" (BDPA 10462) cultivar has red fruits, the "Yantarnyi" (BDPA 14131) and "Flava" (BDPA 8795) cultivars have yellow fruits. Unfortunately, cornelian cherry is rarely used in Ukraine.

The effects of fruits of different cultivars of this species *in vivo* in diabetes have not been adequately studied to date. Because of this, the aim of the study was to evaluate the impact of biologically active substances present in fruit extracts of different cultivars of *Cornus mas* L. on the content of triacylglycerols, cholesterol, HDL-C and LDL-C in blood plasma of rats with streptozotocin-induced DM.

MATERIALS AND METHODS

Wistar male rats with starting weight of 140–170 g were used for all experiments. Rats were kept in the vivarium with standard conditions in accordance with "General ethical principles of experimentation on animals" approved by the First National Congress on Bioethics (Kyiv, Ukraine, 2001) and the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, France, 1985). The bioethical examination of the experiments carried out at the Biological Faculty of the Ivan Franko National University of Lviv was executed in the form of a protocol No. 30-02-2023 of January 10, 2023. Experimental type 1 DM was induced by intraperitoneal injection of streptozotocin (Sigma-Aldrich, St. Louis, MO, USA) freshly prepared as a solution in 10 mM citrate buffer (pH 4.5) at the rate of 55 mg/kg of animal body weight. The development of diabetes was monitored by the content of glucose in the blood, the level of which was determined on days 3 and 10 after the injection of streptozotocin. For this, blood was sampled from the tail vein of the animals and the glucose concentration was determined using an analytical kit for the enzymatic determination of glucose from the company "Filisit-Diagnostyka" (Dnipro, Ukraine). Rats having blood glucose concentration over 12–14 mmol/L were considered as diabetic and used for further experiments.

The animals were divided into five groups. The first (control) and the second (diabetic control) groups received by gavage 1 mL/rat of water once daily for 14 days. Diabetic animals of the third group were orally administered 1 mL/rat the extract of the fruits of the "Podolski" cultivar (ripe red fruits) of *Cornus mas* L., the fourth group – the extract of the fruits of the "Yantarnyi" cultivar (ripe yellow fruits), the fifth group – the "Loganic acid" extract, extracted from yellow fruits of the "Yantarnyi" and "Flava" cultivars of *Cornus mas* L., at a dose of 20 mg/kg of body weight for 14 days. The dose and duration of administration were selected based of previous studies (Dzydzan *et al*., 2019, 2020). Procedures for the preparation of the cornelian cherry extracts, identification and

quantification of compounds of extracts by the UPLC-qTOF-MS/MS and HPLC-PDA methods were described by O. Dzydzan *et al.* (Dzydzan *et al*., 2019, 2020).

After 14 days of administration of the cornelian cherry extracts, the rats were anesthetized using diethyl ether and euthanized by decapitation. Blood was collected into vials with heparin (final dilution heparin: whole blood = 1:100). Before blood sampling, heparin (5000 units/mL) was diluted with physiological solution (0.9% NaCl solution) in the ratio of 1:5. The blood was centrifuged for 15 min at 3000 rpm to obtain plasma. In the obtained plasma samples, the main markers of the lipid profile (content of triacylglycerols, cholesterol and its esters, LDL-C, HDL-C) were determined using analytical kits "Filisit-Diagnostyka" (Dnipro, Ukraine). The levels of triglycerides (TG) and total cholesterol (Total CHOL) were estimated based on calorimetric, enzymatic methods. HDL-C and LDL-C were measured using calorimetric, direct methods. Based on the obtained experimental results of changes in plasma lipid profile, atherogenicity indices (AI) were calculated (Atherogenic Index of Plasma (AIP), Castelli's risk index I, Castelli's risk index II, atherogenic coefficient (AC) and CHOLIndex).

The AIP was calculated by means of the Log_{10} (TG/HDL-C). This index reflects the levels of TG and HDL-C. The calculation of Castelli's risk index (CRI) is based on three important parameters of the lipid profile, i.e. Total CHOL, LDL-C and HDL-C. It is divided into two CRI categories: CRI-I and CRI-II. The CRI-I was established based on the ratio of Total CHOL and HDL-C (CRI-I = Total CHOL/HDL-C). The CRI-II was calculated as the ratio of LDL-C to HDL-C (CRI-II = LDL-C/HDL-C). The AC was calculated according to the formula: {(Total CHOL – HDL-C)/HDL-C}, and CHOLIndex – according to the formula: CHOLIndex = LDL-C – HDL-C (Akpinar *et al*., 2013; Dobiášová & Frohlich, 2001; Kamoru *et al*., 2017; Sozański *et al*., 2016).

Statistical analysis of the results was performed using Microsoft Excel 2013 (Microsoft, Redmond, WA, USA). The main statistical indicators were calculated based on direct quantitative data obtained as a result of research. The results were expressed as mean ± standard error of the mean (M ± SEM). To assess the probability of the difference between the statistical characteristics of two data sets, the Student's coefficient was calculated. Differences between the groups were considered statistically significant at $P \leq 0.05$.

RESULTS AND DISCUSSION

Dyslipidemia is considered a common metabolic disorder associated with diabetes – qualitative and quantitative changes in blood plasma lipids and lipoproteins. One of the manifestations of diabetic dyslipidemia is hypercholesterolemia (increased level of total cholesterol) and hypertriglyceridemia (increased level of triacylglycerols) (Wu & Parhofer, 2014).

Analysis of changes in the total amount of cholesterol in the blood plasma of the experimental animals showed an increase in its concentration compared to the control group of animals (**Fig. 1*A***). Hypercholesterolemia is often associated with an increased risk of cardiovascular disease, including atherosclerosis, in both diabetic and non-diabetic patients. There are isolated endogenous (synthesized *de novo* in the body from the precursor compound acetyl-CoA) and exogenous cholesterol (contained in food products) (Soliman, 2018). Since only maintaining the glucose concentration within the normal level for diabetes does not significantly prevent the development of complica-

tions and reduce mortality, it is also important to adjust the levels of blood plasma lipids, particularly cholesterol (Wu & Parhofer, 2014).

The administration of extracts of the red fruits of *Cornus mas* L. and "Loganic acid" in diabetic animals caused a significant decrease in the concentration of cholesterol in the blood plasma (**Fig. 1*A***). The ability of the extracts of the red fruits of *Cornus mas* L. and "Loganic acid" to reduce the level of cholesterol may be due to the inhibitory effect of iridoids (due to the administration of "Loganic acid") (Dzydzan *et al.*, 2020) and phenolic compounds – flavonoids and anthocyanins, which are one of the main bioactive compounds in the composition of extract of red fruit of *Cornus mas* L. (Dzydzan *et al.*, 2019), – on the activity of β-hydroxy-β-methylglutaryl-CoA reductase. This enzyme is a key regulatory enzyme involved in the mevalonate pathway of cholesterol synthesis (Hosseinpour *et al.*, 2017).

Fatty acids, which, like glucose, are the main source of energy for body tissues, form triesters with glycerol – triacylglycerides, which are the main form of energy storage in adipocytes. Triacylglycerides also ensure the transport of esterified fatty acids as part of chylomicrons (Alexopoulos *et al.*, 2019).

As a result of the study of the content of triglycerides in the blood plasma of experimental animals, we found that their content significantly increases under diabetes (**Fig. 1*B***). Diabetic hypertriglyceridemia is a significant risk factor for the development of complications in patients with diabetes. The search for therapeutic agents that make it possible to reduce the level of triacylglycerols in the blood plasma is one of medical and biological research priority areas.

Administration of the "Loganic acid" extract to animals with diabetes caused a significant decrease in the concentration of triacylglycerols compared to the concentration of these lipids in the blood plasma of diabetic animals (**Fig. 1*B***).

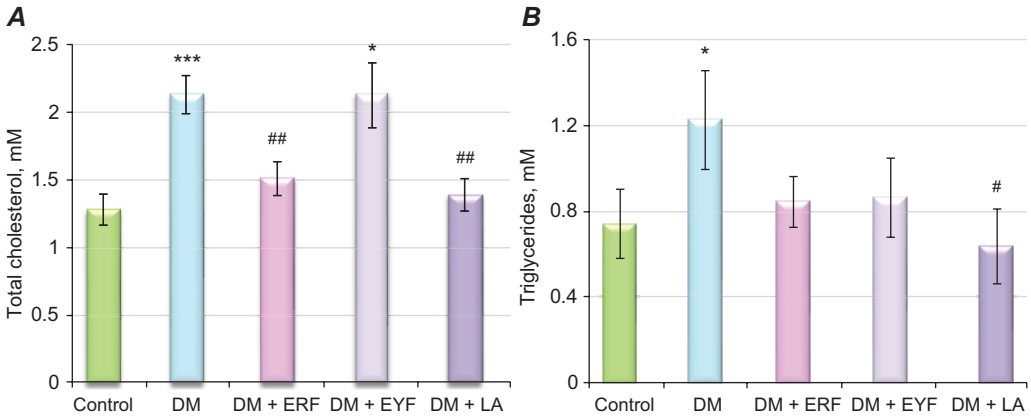

Fig. 1. The levels of total cholesterol (***A***) and triacylglycerols (***B***) in blood plasma of control rats, under diabetes mellitus (DM) and after treatment with extracts of red (ERF) and yellow (EYF) fruits of *Cornus mas* L., and "Loganic acid" (LA), extracted from yellow fruits of cornelian cherry. *Designations*. Compared to the control group: * – $P < 0.05$; *** – $P < 0.001$; compared to the DM group: # – $P < 0.05$; ## – $P < 0.01$

The result of the experiment gives reason to assume that the confirmed hypotriglyceridemic effect of the "Loganic acid" extract alone may be due to the high content of iridoids in this extract compared to the other tested extracts. It should be noted that the

amount of loganic acid was 97.6 % of the total amount of bioactive compounds in this extract (Dzydzan *et al*., 2020).

Loganic acid and its methyl derivative – loganin – belong to the group of iridoid glycosides. The main sources of loganic acid are fruits, including the fruits of *Cornus mas* L. Iridoid glycosides exhibit different pharmacological effects (antibiotic, anti-inflammatory, hypotensive) depending on their molecular structure. Loganic acid exhibits a hypoglycemic effect due to the presence of functional islets of Langerhans in the pancreas. Glucagon-like peptide-1 is known to stimulate pancreatic β-cell insulin secretion, in addition to its ability to increase glucose-stimulated insulin secretion (Davies *et al*., 2019). The main protein targets of loganic acid, which it will most likely affect, are adenosine receptor type A1 and carbonic anhydrase II (Tang *et al*., 2018). Therefore, loganic acid, showing antioxidant properties, can have a beneficial effect on the body of people with diabetes. Such results suggest that loganic acid is one of the plant components in the development of new drugs that will correct the metabolism and functional disorders in DM (Davies *et al*., 2019).

Other important indicators of the lipid profile are the concentration of HDL-C and LDL-C. Lipoproteins are protein-lipid complexes that transport lipids in the blood plasma. According to the content of proteins (apolipoproteins) and lipid components, they are divided into HDL-C that contain a large proportion of protein (45–50 %) and, accordingly, have a higher relative density, and LDL-C that contain a small amount of protein (8–20 %) and, on the other hand, a significant amount of lipids, which is why they have a lower relative density. HDL-C reduces the risk of the formation of atherosclerotic plaques, as they contribute to the removal of cholesterol, transporting it from peripheral tissues (including macrophages in the walls of blood vessels) to the liver, where it undergoes further metabolic transformations. LDL-C, due to their ability to undergo an alternative type of catabolism (oxidation), are atherogenic. An increase in the content of LDL-C in the blood plasma causes hypercholesterolemia and intensifies their breakdown in an alternative way (Sybirna *et al.,* 2018).

Therefore, a decrease in the content of HDL-C and an increase in the content of LDL-C in diabetes are critical manifestations of dyslipidemia and factors that complicate the patient's condition. Such changes in the lipid profile make it important to search for therapeutic agents that would correct the levels of these lipoproteins.

Under experimental diabetes the content of HDL-C in blood plasma is significantly reduced compared to the control group (**Fig. 2*A***). The insulin-deficient state due to diabetes affects the activity of liver enzymes involved in the catabolism of HDL-C, which leads to an increased breakdown of the corresponding lipoproteins (Vergès, 2015).

Under administration of extracts of fruits of Cornus mas L. reliable changes were detected only in the group of animals that received the "Loganic acid" extract (**Fig. 2*A***). The ability of loganic acid to increase the concentration of HDL-C in blood plasma may be due to the effect of iridoids on transcription factors involved in intracellular signaling pathways, especially those involved in the synthesis of apolipoproteins that are part of these lipid-protein complexes (Danielewski *et al*., 2021).

LDL-C enters cells from blood plasma by insulin-regulated receptor-mediated endocytosis (Vergès, 2015). Due to the fact that under diabetes there is a marked hypoinsulinemia, as a result of which the expression and activity of the corresponding receptors decrease, the content of LDL-C increased in the blood plasma of the diabetic

group (**Fig. 2*B***). Administration of the "Loganic acid" extract to animals with streptozotocin-induced DM caused a decrease in the content of LDL-C to the values in the control group of animals (**Fig. 2*B***).

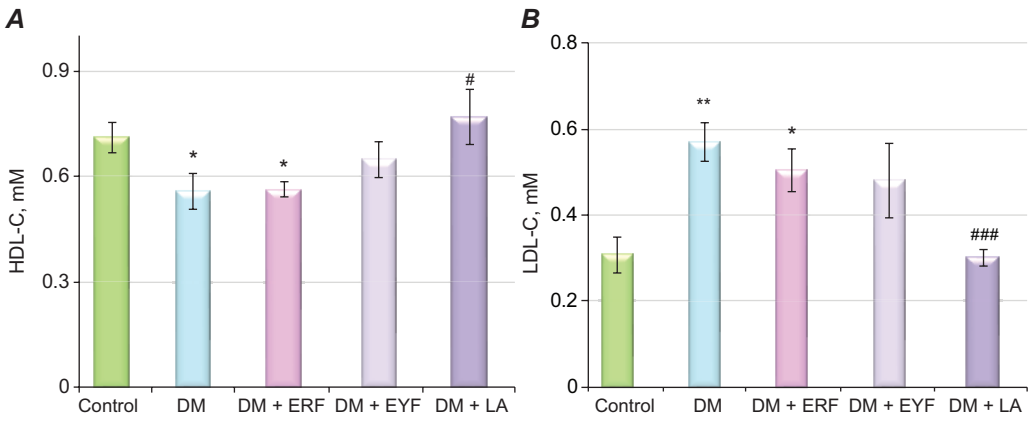

Fig. 2. The effect of cornelian cherry fruit extracts on the content of HDL-C (***A***) and LDL-C (***B***) in the blood plasma of rats with streptozotocin-induced diabetes. *Designations*. Compared to the control group: * – P < 0.05; ** – P < 0.01; compared to the DM group: # – P < 0.05; ### – P < 0.001

Based on changes in the concentration of LDL-C and HDL-C, triglycerides and total cholesterol, atherogenicity indices were calculated, which make it possible to assess the degree of risk of cardiovascular complications in diabetes (**Fig. 3–6**). Although the lipid-lowering effects of loganic acid were stronger than the effects exerted by extracts of red fruit *Cornus mas* L., the trend in lipidogram changes produced by both constituents was similar.

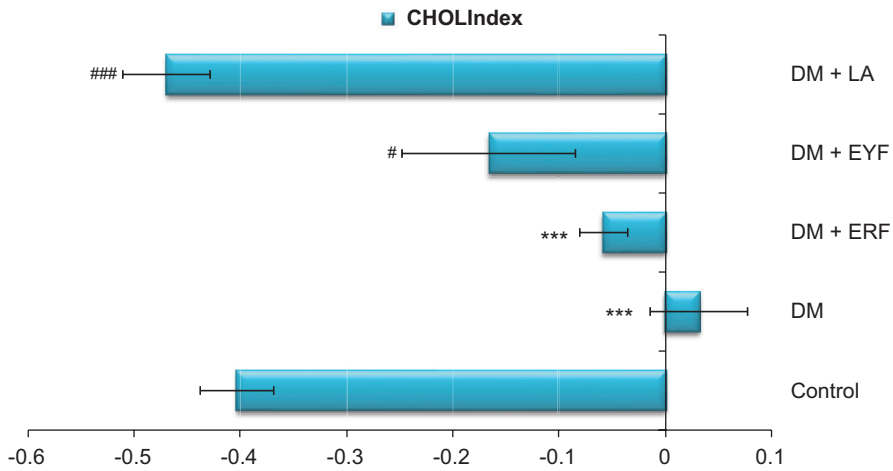

Fig. 3. CHOLIndex, calculated on the basis of the difference between LDL-C and HDL-C, in control, under DM and the administration of extracts of fruits of *Cornus mas* L. *Designations*. Compared to the control group: *** – P < 0.001; compared to the DM group: # – P < 0.05; ### – P < 0.001

The CHOLIndex had a much more significant correlation with coronary artery disease compared with other lipid parameters. The CHOLIndex value in the red and yellow cornelian cherry-treated group of DM was significantly lower than in the diabetic group (**Fig. 3**), despite the fact that the LDL-C and HDL-C levels did not reach significant differences in this group of animals compaired to DM group (see **Fig. 2**).

Castelli's risk index I and Castelli's risk index II make it possible to predict the risk of coronary plaques. A significant decrease in the values of these indices (**Fig. 4**) after the treatment of animals with streptozotocin-induced diabetes with extracts of *Cornus mas* L. fruits, and especially after the introduction of the "Loganic acid" extract, indicates a decrease in the risk of developing coronary complications.

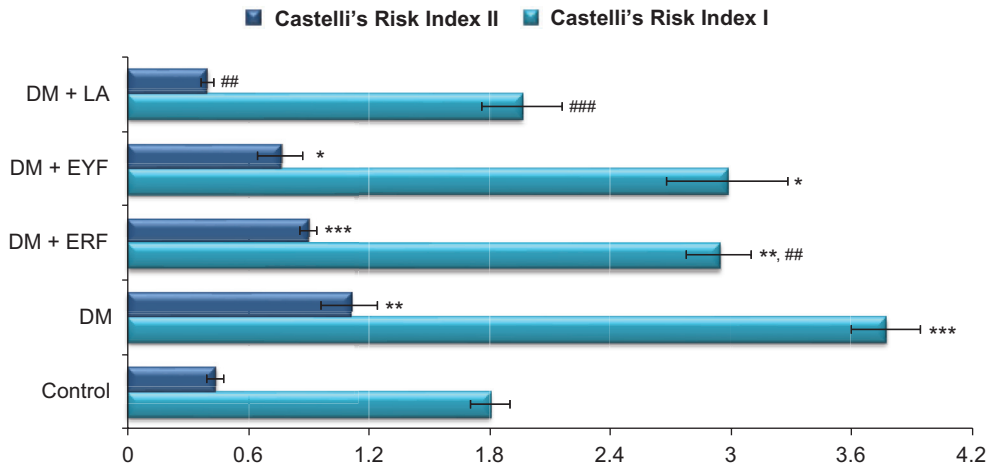

Fig. 4. Castelli's risk index I and Castelli's risk index II calculated on the basis of three important parameters of the lipid profile (Total CHOL, LDL-C and HDL-C), in control, under DM and the administration of extracts of fruits of *Cornus mas* L. *Designations*. Compared to the control group: * – P < 0.05; ** – P < 0.01; *** – P < 0.001; compared to the DM group: ## – P < 0.01; ### – P < 0.001

The Castelli's risk index values in both the DM + ERF and DM + EYF group were significantly lower compared to the diabetic group, but still higher than in the control group and in the animals after the administration of the "Loganic acid" extract.

Analyzing the direction of changes Atherogenicity coefficient (**Fig. 5**), we found that the atherogenic potential of the lipoprotein fractions of the blood plasma significantly decreases with the administration of extracts of fruits *Cornus mas* L. to animals with diabetes.

A significant decrease in the Atherogenic Index of Plasma (**Fig. 5**) in the groups of animals that received extracts of cornelian cherry fruits, and especially after the administration of the "Loganic acid" extract, indicates the manifestation of hypolipidemic properties of the extracts under study. The fruits of *Cornus mas* L., especially those cultivars that are enriched with iridoid glycoside – loganic acid, can be recommended as an additional treatment for lowering the level of cholesterol and triglycerides in the blood.

Loganic acid completely reversed the Atherogenic Index of Plasma. Its level was significantly lower compared to the DM group, and still lower than in the control group.

Thus, it is important to estimate lipid indices, especially because half of all cardiovascular events develop even when the levels of lipids in plasma are within the normal range. The investigated extracts of *Cornus mas* L. significantly decreased lipid indexes that predict the risk of atherosclerosis and cardiac complications. Loganic acid exerted more pronounced effects than extracts of red and yellow fruits of *Cornus mas* L., especially in decreasing the Atherogenicity coefficient, Castelli's risk indexs and CHOLIndex to levels similar to the control group. Moreover, Atherogenic Index of Plasma value in the loganic acid-treated group of DM was lower than in the control group.

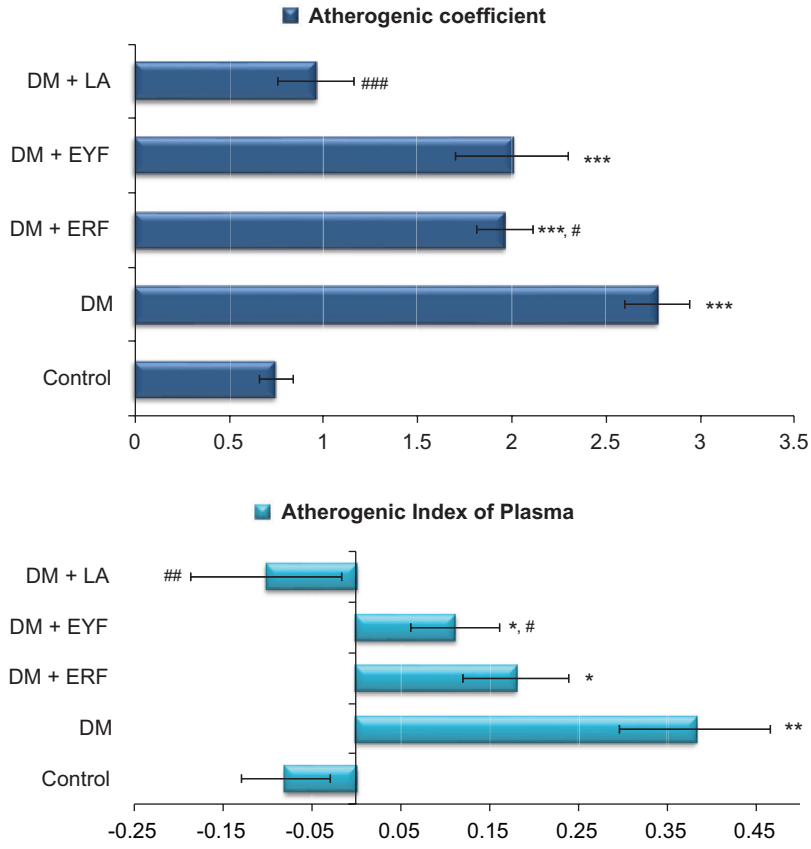

Fig. 5. Atherogenicity coefficient calculated on the basis of changes in the content of Total CHOL, LDL-C and HDL-C, and the atherogenicity index calculated on the basis of changes in the content of TG and HDL-C in the blood plasma, in control, under DM and the administration of extracts of fruits of *Cornus mas* L. *Designations*. Compared to the control group: * – $P < 0.05$; ** – $P < 0.01$; *** – $P < 0.001$; compared to the DM group: # – $P < 0.05$; ## – $P < 0.01$; ### – $P < 0.001$

Therefore, the reduction of all atherogenicity indices in groups of rats that were treated with fruit extracts of different cultivars of *Cornus mas* L., compared to animals with streptozotocin diabetes, indicates a decrease in the risk of cardiovascular complications under the studied pathology in an animal model (**Fig. 6**).

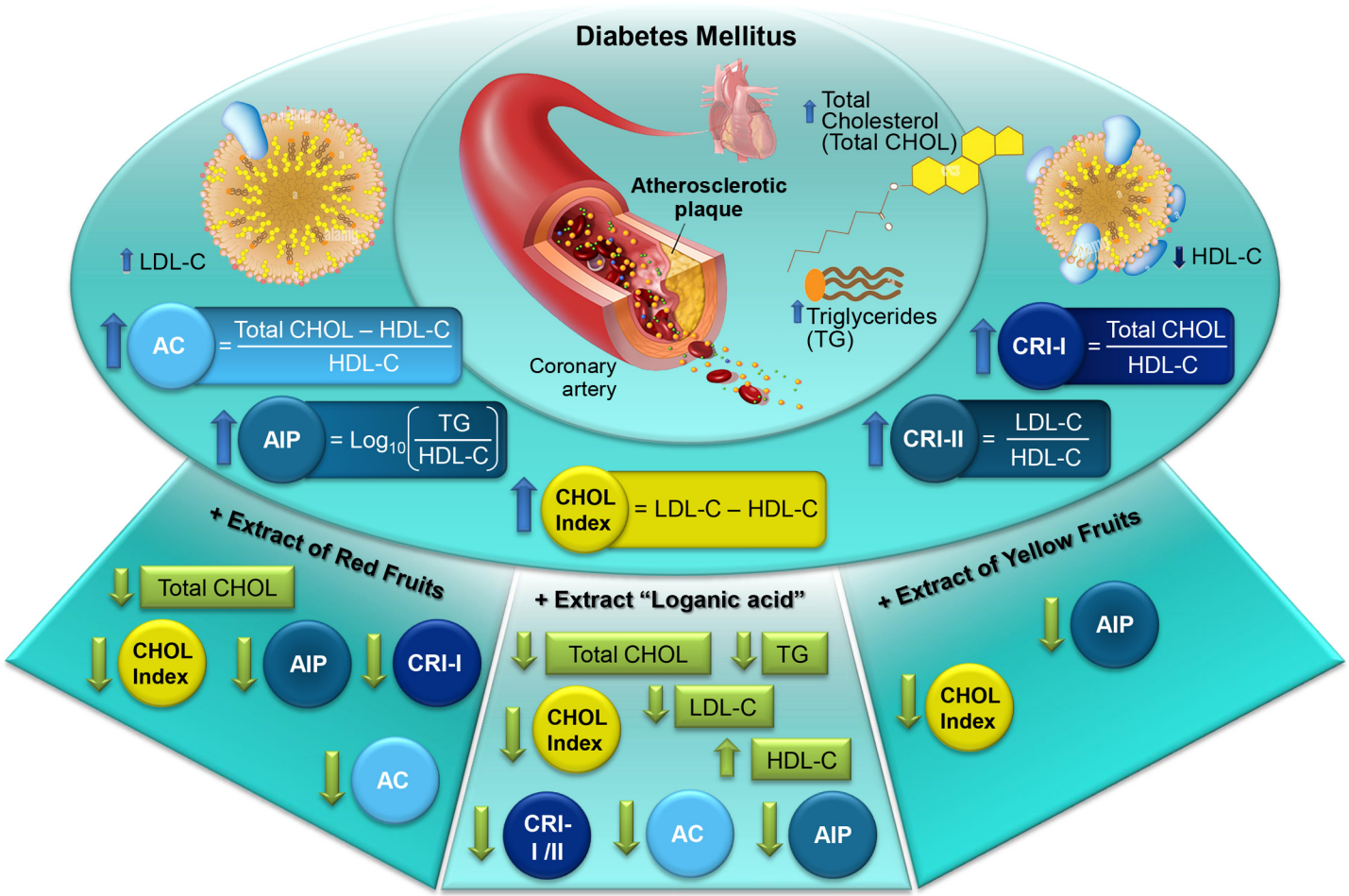

Fig. 6. Scheme of the effect of extracts of fruits of different cultivars of *Cornus mas* L. on plasma lipid profile of rats with streptozotocin-induced diabetes mellitus

CONCLUSIONS

It was found that the administration extracts of fruits of *Cornus mas* L. for 14 days to animals with streptozotocin-induced diabetes causes positive changes in the lipid profile of the blood plasma, preventing the possibility of the development of atherosclerotic changes in diabetes. The extract of the red fruits of the "Podolski" cultivar led to a significant decrease only in the content of cholesterol in the blood plasma of rats with streptozotocin diabetes. Administration of the "Loganic acid" extract obtained from the yellow fruits of cornelian cherry "Yantarnyi" and "Flava" cultivars to animals with diabetes led to a decrease in the concentration of total cholesterol, triglycerides, and the content of LDL-C against the background of an increase in the content of HDL-C. Atherogenic indices calculated on the basis of changes in the concentration of LDL-C, HDL-C, triglycerides and total cholesterol made it possible to conclude that the degree of risk of cardiovascular complications in diabetes is significantly reduced against the background of the administration of cornelian cherry fruit extracts. Our results indicate that *Cornus mas* L. fruit extracts may be a potential therapeutic agent or dietary supplement for dyslipidemias, especially under type 1 diabetes.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Human Rights: This article does not contain any studies with human subjects performed by the any of the authors.

Animal studies: All institutional and national guidelines for the care, maintenance and use of laboratory animals were followed.

AUTHOR CONTRIBUTIONS

Conceptualization, [B.I.V.]; methodology, [C.A.Z., B.I.V., C.M.O.]; investigation, [C.A.Z., C.M.O., M.A.A.]; data analysis, [B.I.V., C.A.Z., C.M.O.]; writing – original draft preparation, [C.M.O., M.A.A.]; writing – review and editing, [B.I.V.]; visualization, [B.I.V.]; supervision, [B.I.V.]; project administration, [C.A.Z., S.N.O.]; funding acquisition, [–].

All authors have read and agreed to the published version of the manuscript.

REFERENCES

Akpınar, O., Bozkurt, A., Acartürk, E., & Seydaoğlu, G. (2013). A new index (CHOLINDEX) in detecting coronary artery disease risk. *Anadolu Kardiyoloji Dergisi/The Anatolian Journal of Cardiology*, 13(4), 315–319. doi:10.5152/akd.2013.098
Crossref ● PubMed ● Google Scholar

Alexopoulos, A.-S., Qamar, A., Hutchins, K., Crowley, M. J., Batch, B. C., & Guyton, J. R. (2019). Triglycerides: emerging targets in diabetes care? Review of moderate hypertriglyceridemia in diabetes. *Current Diabetes Reports*, 19(4), 13. doi:10.1007/s11892-019-1136-3
Crossref ● PubMed ● PMC ● Google Scholar

Danielewski, M., Matuszewska, A., Szeląg, A., & Sozański, T. (2021). The impact of anthocyanins and iridoids on transcription factors crucial for lipid and cholesterol homeostasis. *International Journal of Molecular Sciences*. 22(11), 6074. doi:/10.3390/ijms22116074
Crossref ● PubMed ● PMC ● Google Scholar

Davies, L. C., Rice, C. M., McVicar, D. W., & Weiss, J. M. (2018). Diversity and environmental adaptation of phagocytic cell metabolism. *Journal of Leukocyte Biology*, 105(1), 37–48. doi:10.1002/jlb.4ri0518-195r
Crossref ● PubMed ● PMC ● Google Scholar

Dobiášová, M., & Frohlich, J. (2001). The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate inapob-lipoprotein-depleted plasma (FER_{HDL}). *Clinical Biochemistry*, 34(7), 583–588. doi:10.1016/s0009-9120(01)00263-6
Crossref ● PubMed ● Google Scholar

Dzydzan, O., Bila, I., Kucharska, A. Z., Brodyak, I., & Sybirna, N. (2019). Antidiabetic effects of extracts of red and yellow fruits of cornelian cherries (*Cornus mas* L.) on rats with streptozotocin-induced diabetes mellitus. *Food & Function*, 10(10), 6459–6472. doi:10.1039/c9fo00515c
Crossref ● PubMed ● Google Scholar

Dzydzan, O., Brodyak, I., Sokół-Łętowska, A., Kucharska, A. Z., & Sybirna, N. (2020). Loganic acid, an iridoid glycoside extracted from *Cornus mas* L. fruits, reduces of carbonyl/oxidative stress biomarkers in plasma and restores antioxidant balance in leukocytes of rats with streptozotocin-induced diabetes mellitus. *Life*, 10(12), 349. doi:10.3390/life10120349
Crossref ● PubMed ● PMC ● Google Scholar

Dzydzan, O., Brodyak, I., Strugała-Danak, P., Strach, A., Kucharska, A. Z., Gabrielska, J., & Sybirna, N. (2022). Biological activity of extracts of red and yellow fruits of *Cornus mas* L. – an *in vitro* evaluation of antioxidant activity, inhibitory activity against α-glucosidase, acetylcholinesterase, and binding capacity to human serum albumin. *Molecules*, 27(7), 2244. doi:10.3390/molecules27072244
Crossref ● PubMed ● PMC ● Google Scholar

Efenberger-Szmechtyk, M., Nowak, A., Czyżowska, A., Kucharska, A. Z., & Fecka, I. (2020). Composition and antibacterial activity of *Aronia melanocarpa* (Michx.) Elliot, *Cornus mas* L. and *Chaenomeles superba* Lindl. leaf extracts. *Molecules*, 25(9), 2011. doi:10.3390/molecules25092011
Crossref ● PubMed ● PMC ● Google Scholar

Hosseinpour, F., Shomali, T., & Rafieian-Kopaei, M. (2017). Hypocholesterolemic activity of cornelian cherry (*Cornus mas* L.) fruits. *Journal of Complementary and Integrative Medicine*, 14(4). doi:10.1515/jcim-2017-0007
Crossref ● PubMed ● Google Scholar

Kamoru, A. A., Japhet, O. M., Adetunji, A. D., Musa, M. A., Akinlawon, A. A., Abdufatah, O. A., Taofik, A. A., & Kabiru, A. A. (2017). Castelli risk index, atherogenic index of plasma, and atherogenic coefficient: emerging risk predictors of cardiovascular disease in HIV-treated patients. *Saudi Journal of Medical and Pharmaceutical Sciences*, 3(10), 1101–1110.
Google Scholar

Kuchurka, O. M., Chaban, M. O., Dzydzan, O. V., Brodyak, I. V., & Sybirna, N. O. (2022). Leukocytes in type 1 diabetes mellitus: the changes they undergo and induce. *Studia Biologica*, 16(1), 47–66. doi:10.30970/sbi.1601.674
Crossref ● Google Scholar

Seniv, M. B., Dzydzan, O. V., Brodyak, I. V., Kucharska, A. Z., & Sybirna, N. O. (2021). Antioxidant effect of extract of yellow fruits of cornelian cherry (*Cornus mas* L.) in rats' leukocytes under streptozotocin-induced diabetes mellitus. *Studia Biologica*, 15(1), 15–26. doi:10.30970/sbi.1501.645
Crossref ● Google Scholar

Soliman, G. (2018). Dietary cholesterol and the lack of evidence in cardiovascular disease. *Nutrients*, 10(6), 780. doi:10.3390/nu10060780
Crossref ● PubMed ● PMC ● Google Scholar

Sozański, T., Kucharska, A. Z., Rapak, A., Szumny, D., Trocha, M., Merwid-Ląd, A., Dzimira, S., Piasecki, T., Piórecki, N., Magdalan, J., & Szeląg, A. (2016). Iridoid – loganic acid *versus* anthocyanins from the *Cornus mas* fruits (cornelian cherry): common and different effects on diet-induced atherosclerosis, PPARs expression and inflammation. *Atherosclerosis*, 254, 151–160. doi:10.1016/j.atherosclerosis.2016.10.001
Crossref ● PubMed ● Google Scholar

Sybirna, N. O. (Ed.), Hachkova, G. Ya., Brodyak, I. V., Sybirna, K. A., Khokhla, M. R., Sabadashka, M. V. (2018). *Funktsionalna biokhimiia* [*Functional biochemistry*]. Lviv: Ivan Franko National University of Lviv. (In Ukrainian)

Tang, C., Li, H.-J., Fan, G., Kuang, T.-T., Meng, X.-L., Zou Z.-M., & Zhang, Y. (2018). Network pharmacology and UPLC-Q-TOF/MS studies on the anti-arthritic mechanism of *Pterocephalus hookeri*. *Tropical Journal of Pharmaceutical Research*, 17(6), 1095–1110. doi:10.4314/tjpr.v17i6.17
Crossref ● Google Scholar

Vergès, B. (2015). Pathophysiology of diabetic dyslipidaemia: where are we? *Diabetologia*, 58(5), 886–899. doi:10.1007/s00125-015-3525-8
Crossref ● PubMed ● PMC ● Google Scholar

Wu, L., & Parhofer, K. G. (2014). Diabetic dyslipidemia. *Metabolism*, 63(12), 1469–1479. doi:10.1016/j.metabol.2014.08.010
Crossref ● PubMed ● Google Scholar

Zhang, P., Li, T., Wu, X., Nice, E. C., Huang, C., & Zhang, Y. (2020). Oxidative stress and diabetes: antioxidative strategies. *Frontiers of Medicine*, 14(5), 583–600. doi:10.1007/s11684-019-0729-1
Crossref ● PubMed ● Google Scholar

ВПЛИВ ЕКСТРАКТІВ ПЛОДІВ РІЗНИХ СОРТІВ ДЕРЕНУ СПРАВЖНЬОГО (*CORNUS MAS* L.) НА ЛІПІДНИЙ ПРОФІЛЬ ПЛАЗМИ ЗА ЕКСПЕРИМЕНТАЛЬНОГО ЦУКРОВОГО ДІАБЕТУ

***І. В. Бродяк*[1] *, М. О. Чабан*[1]*, А. А. Мороз*[1]*, А. З. Кучарська*[2]*, Н. О. Сибірна*[1]**

[1] *Львівський національний університет імені Івана Франка, вул. Грушевського, 4, Львів 79005, Україна*

[2] *Вроцлавський університет природничих наук, вул. Ю. Хелмонського, 37/41, 51-630 Вроцлав, Польща*

Вступ. Цукровий діабет (ЦД), одночасно з порушеним транспортом глюкози з крові у клітини на тлі абсолютної чи відносної гіпоінсулінемії, супроводжується розвитком дисліпідемії. Відтак, істотне значення має пошук терапевтичних засобів, здатних полегшувати симптоми і, як наслідок, перебіг ЦД. Скринінг антидіабетичних засобів вказує на те, що одним з їхніх основних потенційних джерел є натуральні продукти рослинного походження. Проте, хоча відомий широкий спектр рослинних екстрактів, які використовуються для лікування діабету, застосування лише окремих з них є науково аргументованим. Тому метою роботи було дослідити вплив біологічно активних речовин, наявних у складі екстрактів плодів різних сортів дерену справжнього, на ліпідний профіль плазми крові за експериментального ЦД.

Матеріали та методи. У дослідженні використовували щурів-самців лінії Wistar масою тіла 140–170 г. Діабет індукували внутрішньоочеревинним введенням стрептозотоцину (55 мг/кг маси тіла). Тварини було поділено на п’ять груп.

Перша (контроль) та друга (ЦД) групи впродовж 14 днів перорально отримували питну воду об'ємом 1 мл. Тваринам з ЦД третьої–п'ятої груп перорально вводили екстракти червоних і жовтих плодів дерену та екстракт "Логанова кислота", відповідно, у дозі 20 мг/кг маси тіла впродовж 14 днів об'ємом 1 мл. У плазмі крові щурів визначали концентрацію ліпопротеїнів низької щільності, ліпопротеїнів високої щільності, тригліцеридів і холестеролу. На основі даних ліпідного профілю плазми крові розраховували індекси атерогенності.

Результати. У разі введення екстракту червоних плодів дерену справжнього сорту "Podolski" у плазмі крові щурів зі стрептозотоциновим діабетом достовірно знижувався вміст загального холестеролу. Екстракт "Логанова кислота", отриманий з жовтих плодів дерену справжнього сортів "Yantarnyi" і "Flava", зумовлював зниження у плазмі крові концентрації загального холестеролу, тригліцеридів і вмісту ліпопротеїнів низької щільності на тлі підвищення вмісту ліпопротеїнів високої щільності. Індекси атерогенності дали змогу встановити, що ступінь ризику виникнення серцево-судинних ускладнень за ЦД значно знижується на тлі введення екстрактів плодів дерену справжнього.

Висновки. Екстракти плодів дерену справжнього сортів "Podolski", "Yantarnyi" і "Flava" коригують ліпідний профіль плазми крові тваринам зі стрептозотоцин-індукованим ЦД та, як наслідок, запобігають розвиткові атеросклеротичних змін і серцево-судинних ускладнень. Плоди *Cornus mas* L. можуть бути потенційними засобами у терапії дисліпідемії за ЦД.

Ключові слова: цукровий діабет, ліпопротеїни низької щільності, ліпопротеїни високої щільності, тригліцериди, холестерол, дисліпідемія, екстракти плодів дерену справжнього (*Cornus mas* L.)

Received / Одержано 12 January, 2023 | Revision / Доопрацьовано 05 February, 2023 | Accepted / Прийнято 22 March, 2022 | Published / Опубліковано 29 March, 2022