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EFFECTS OF STANDARDIZED *ARONIA MELANOCARPA* EXTRACT ON CARDIOVASCULAR SYSTEM: FROM BASIC TO APPLIED INVESTIGATION

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Abstract: This study summarizes the effects standardized Aronia melanocarpa extract (SAE) on different pathophysiological processes linked with cardiovascular system from both animal and human investigations. In basic researches we estimated the influence of SAE on rats with metabolic syndrome (MetS) and polycystic ovary syndrome (PCOS). Human studies aimed to assess the impact of SAE in patients with MetS and in professional handball players. SAE had the ability to lower blood pressure and exert benefits on *in vivo* and *ex vivo* heart function. Furthermore, SAE induced a wide range of beneficial effects in human researches. Overall, SAE could be a promising strategy to reduce cardiovascular risk.

Keywords: standardized Aronia melanocarpa extract, cardiovascular system, rats, handball players, oxidative stress

Introduction

Aronia melanocarpa (*A. melanocarpa*) or black chokeberry is a fruit/plant which belongs to the *Rosaceae* family and is native to North America (Daskalova, 2015). However, it has been commonly used in Europe as ingredient for juices, wine, jams, teas and cordial liqueurs (Ochmian, 2012). *A. melanocarpa* represents one of the richest sources of polyphenols among fruits, with anthocyanins and flavonoids identified as major components responsible for its therapeutic potential (Cebova, 2017). Recent researches have focused attention on *A. melanocarpa* due to its numerous health benefits in a broad range of pathological conditions (Jurikova, 2017). It has been reported that fruit and extracts of *A. melanocarpa* exert gastroprotective, hepatoprotective, antiinflammatory and antiproliferative activity (Lupascu, 2016). Furthermore,

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the health-promoting effects of extracts of this plant involve antiatherosclerotic, antiplatelet and hypoglycemic properties (Borowska, 2016). However researches of standardized extract of this plant have not been yet investigated both on animal and human models.

This study summarizes the effects standardized Aronia melanocarpa extract (SAE) on different pathophysiological processes linked with cardiovascular system from both animal and human investigations.

Materials and methods

Ethical aspects

The protocol was approved by the Ethical Committees for animal (119-01-5/14/2017-09) and human investigations (03256/2016).

Study design

The study includes a wide range of research on animal models and on human population.

1. In the first part of the study we examined the effects of different dietary strategies, high-fat (HFd) or standard diet (Sd) alone or in combination with standardized oral supplementation (0.45 mL/kg/day) of Aronia melanocarpa extract (SAE) in rats with metabolic syndrome (MetS). SAE is an official product of pharmaceutical company Pharmanova (Belgrade, Serbia). Rats were divided randomly into six groups: control with Sd, control with Sd and SAE, MetS with HFd, MetS with HFd and SAE, MetS with Sd and MetS with Sd and SAE during 4 weeks. At the end of the 4-week protocol, cardiac function and liver morphology were assessed, while in the blood samples glucose, insulin, iron levels and systemic redox state were determined.

2. In the second part of the study we investigated isolated and synergistic effects of Standardized Aronia melanocarpa extract (SEA) and Metformin (MET) for alleviating reproductive and metabolic PCOS abnormalities. PCOS induction was followed by 28-day treatment with MET, SAE, or MET + SEA. Bodyweight (BW), cyclicity, histological, and ultrasonographical ovarian analyses were performed. Hormonal, glycemic, and lipid profiles were accessed, as well as systemic and ovarian oxidative status.

3. In the third part of the study we examine the effect of 4-week supplementation of Alixir 400 PROTECT® (Standardized Aronia L.

Melanocarpa Extract Extract-SAE) on clinical and biochemical parameters in patients with confirmed metabolic syndrome (MetS). This study was designed as a prospective open-label clinical case-series study with 28 days of follow-up with cases selected and followed during the period from February 1, 2018 to November 2019. The study included 143 male and female patients with MetS who were subjected to SAE.

4. In the fourth part we investigated the effects of one-month consumption of polyphenol-rich standardized Aronia melanocarpa extract (SAE) on redox status in anemic hemodialysis patients. The study included 30 patients (Hb < 110 g/l, hemodialysis or hemodiafiltration > 3 months; > 3 times week). Patients were treated with commercially available SAE in a dose of 30 ml/day, for 30 days. After finishing the treatment blood samples were taken to evaluate the effects of SAE on redox status. Several parameters of anemia and inflammation were also followed.

5. In the last part we investigated the influence of twelve-week consumption of chokeberry extract on redox status, body composition, lipid profile and biochemical parameters in active handball players. The study included 16 handball players, aged 16-24 years (20.26±2.86 years). Every morning before training players received 30mL of liquid chokeberry extract for 12 weeks, during regular competition season. The research consisted of morphofunctional and biochemical testing, which was performed at three points (at the beginning of the study, 6 and 12 weeks after extract consumption).

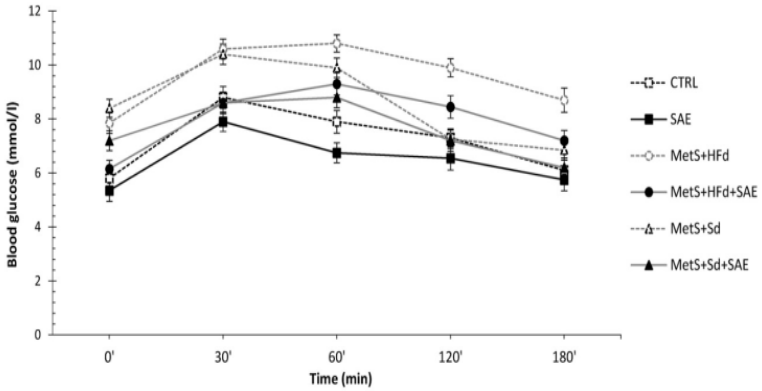
Statistical analysis

Data were collected and analyzed using the Statistical Package for the Social Sciences (SPSS). Descriptive analysis was used to describe results (mean, standard deviation, standard error of mean, frequency in percentage). $\chi 2$ and correlation tests were applied to analyze continuous and categorical variables, respectively. For continuous variables, we used ANOVA for repeated measures (RM-ANOVA). P-value < 0.05 was considered statistically significant.

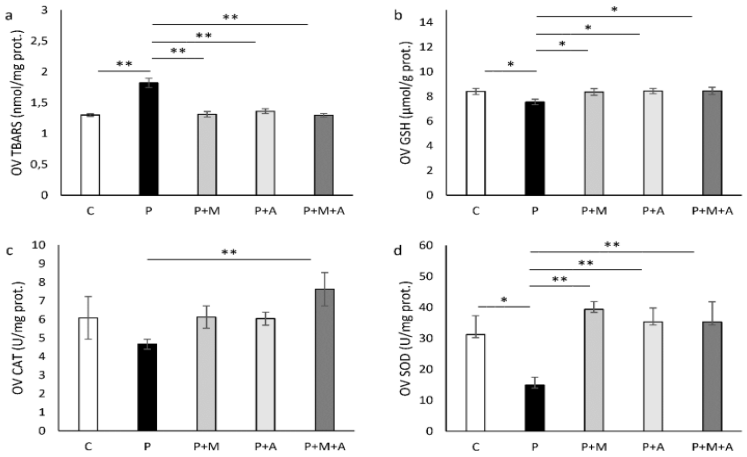
Results and discussion

Results from the first part of the study demonstrated that SAE exert benefits on *in vivo* heart function (Graph 1). Moreover, SAE improved glucose tolerance, attenuated pathological liver alterations and oxidative stress present in MetS. Obtained beneficial effects of SAE were more prominent in combination with changing dietary habits.

In the second part of the study ovarian TBARS levels were increased in the P group ($p < 0.01$) in comparison to the C group. However, treatment with SEA, MET, or their combination decreased these parameter values ($p < 0.01$) compared to the P group (Graph 6a). As shown in Graph 2b, GSH values were decreased in the P group compared to all other investigated groups ($p < 0.05$). CAT activity was increased only in the P + M + A group ($p < 0.01$) compared to the P group (Graph 2c). Ovarian SOD activity was decreased in the P group ($p < 0.05$) in comparison to the C group, and all treated groups showed elevation of SOD compared to the P group ($p < 0.01$), as shown in Graph 2d.



Graph 1. The effects of SAE on glucose levels during OGTT.



Graph 2. Oxidative stress parameters in ovarian tissue

In the third part of the study we found that cholesterol levels significantly decreased in the fMetS-DM group compared to the baseline values in this group, while the LDL levels significantly decreased in the fMetS group. Triglycerides significantly decreased only after 4 weeks of SAE treatment in diabetic groups of patients (fMetS-DM and mMetS-DM) compared to the baseline, while in non-diabetic groups this marker was not significantly altered.

In the fourth part of the study SAE did not improve inflammatory status, except for minor decrease in C-reactive protein. The consumptionof SAE regulates redox status (reduce the productions of pro-oxidative molecules and increase antioxidant defense) and has beneficial effects on anemia parameters.

In the last part of the investigation we noticed that supplementation with chokeberry extract decreased the levels of pro-oxidants (TBARS and nitrites) and increased catalase activity in handball players.

Conclusion

Taken all together, in can be concluded that SAE supplementation was associated with beneficial cardiovascular effects in both animal and human studies through wide range of possible mechanisms such as anti-oxidative potential. Nevertheless all these promising results in triggering cardioprotection should be further examined in future.

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