

## ABSTRACT

### INTRODUCTION:

Metabolic Syndrome (MetS) is not a separate disease but is defined as an array of correlative pathologies comprising central obesity, insulin resistance, hyperglycemia, dyslipidemia, and elevated blood pressure. Their coexistence rise pointedly the risk of cardiovascular diseases (CVD), diabetes mellitus, kidney failure, and liver insufficiency. Novel approach in the therapeutic management constitutes an implementation of polyphenols into the dietary intervention. Pomegranate peels, a by-product of food industry, seem to be a very promising source of these compounds. The present study aimed to evaluate the biological potency of polyphenol-rich pomegranate peel extract in mitigating the main components of metabolic syndrome, especially in the context of cardiovascular system in animal model.

### METHODS:

Zucker Diabetic Fatty rats (ZDF, fa/fa) and their healthy control (fa/+) were supplemented with polyphenol-rich pomegranate peel extract (EPP) in two dosages: 100 mg/kg BW and 200 mg/kg BW for 8 weeks. All individuals had free access to water and a high-calorie diet, Purina 5008. During EPP administration performed body weight and echocardiography measurements. To asses morphology, biochemical parameters and smear image, the blood samples were collected three times. At the end of the study all individuals were euthanized and the heart and aorta sections were harvested. Obtained specimens was used in histology examination and to assess the oxidative status markers (CAT, SOD, MnSOD, GR, GST, GPx, TOS, SH, MDA) and biomarkers of heart failure (cTnI, GAL-3).

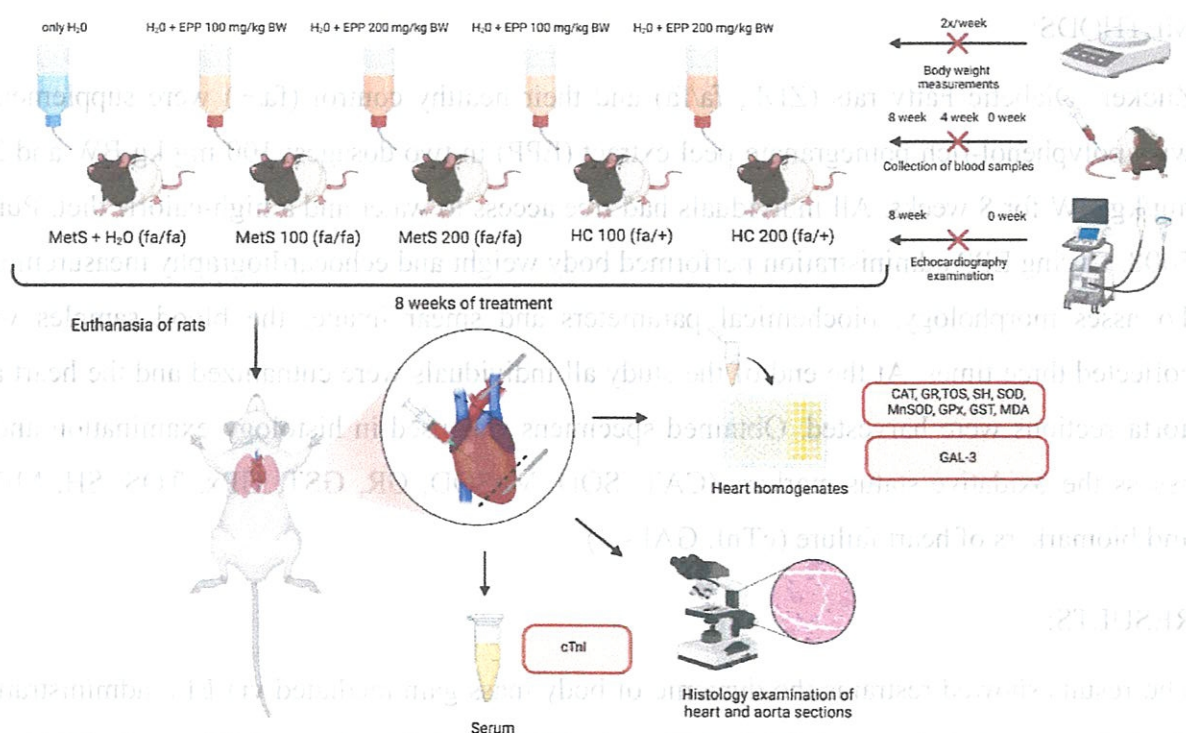
### RESULTS:

The results showed restrains the dynamic of body mass gain mediated via EPP administration. No influence on glucose and lipid profile was determined. The dose of 200 mg/kg BW in the group of rats predisposed to MetS (MetS 200, fa/fa 200) contributed to improvement of cardiac function reflected by increase in mid-wall fractional shortening (mFS, 95% CI: 0.69%-14.61%,  $p=0.032$ ), enhancement of end-diastolic volume of left ventricule (LVEDV, 95% CI: 0.03-0.45,  $p=0.026$ ) and relative decrease in heart rate (HR, 95% CI: -79.29- - 8.38,  $p=0,017$ ). In homogenates of heart tissue the SH concentration increased significantly under the influence of EPP supplementation ( $p<0,001$ ). Moreover, the extract administration in a dose of 100 mg/kg BW conduce to reduction of TOS level more efficiently compared to higher dose ( $p<0.001$ ). The trend in MDA depletion in a dose-dependent manner was observed in rats without genetic

predilection to metabolic syndrome (HC 100: fa/+100, HC 200: fa/+ 200). MetS rats did not follow the same trend. No differences in in GR (P=0,068), SOD (p=0,068), and MnSOD (p=0.363) concentration were observed in groups treated with pomegranate peel extract. The EPP administration did not also affect the cTnI and GAL-3 concentration. In histology examination no toxic alternation was revealed in exposure to applied dosages.

## CONCLUSION:

Phenolic compound from pomegranate peels possess health-promoting properties, chiefly in range of protection cardiovascular system and could be employ in prevention and treatment of Metabolic Syndrome. However, their bioavailability still requires further evaluation in clinical trials in humans.



**Fig. 1** Experimental design. The scheme was created with Biorender.com (accessed on 24.05.2023 r.). Abbreviations: EPP- extract from pomegranate peels, BW- body weight, MetS- metabolic syndrome, fa/fa- rats with mutation in leptin receptor gene predisposed to MetS, fa/+ Zucker rats, healthy control, CAT- catalase, GR- glutathione reductase, TOS- total oxidative status, SH- protein thiol groups, SOD- superoxide dismutase, MnSOD- Mn-dependent superoxide dismutase, GPx- glutathione peroxidase, GST- glutathione transferase, MDA- malondialdehyde, GAL-3- galectin 3, cTnI- troponin I