DOI: 10.46793/SBT29.76AS

BENEFICIAL PROPERTIES OF TRAMETES VERSICOLOR HETEROPOLYSACCHARIDES IN A RAT MODEL OF METABOLIC SYNDROME

Aleksandra Stojanovic[1,2], Marina Nikolic[2,3], Nevena Lazarevic[1,2], Jovana Novakovic[1,2], Nevena Jeremic[1,2,4], Vladimir Zivkovic[2,3,5], Jovana Bradic[1,2], Vladimir Jakovljevic[2,3,6]

Abstract: We aimed to examine the potentially beneficial effects of Trametes versicolor heteropolysaccharides (TVH) on redox balance in a rats with metabolic syndrome (MetS). Total of 40 Wistar rats were divided into 5 groups: CTRL-healthy non-treated rats; MetS-non-treated rats; H-TV (high dose of TV), M-TV (medium dose of TV) and L-TV (low dose of TV)-rats with MetS treated with either 300, 200 or 100 mg/kg TVH per os for 4 weeks. Prooxidative parameters and parameters of the antioxidative defense system were determined spectrophotometrically. H-TV and M-TV significantly reduced the level of prooxidants and increased antioxidants activity. The obtained results demonstrated that the TVH may be considered a potentially useful agent for redox balance in MetS conditions.

Keywords: Trametes versicolor, heteropolysaccharides, antioxidant, metabolic syndrome

[1]Department of Pharmacy, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovica 69, 34000 Kragujevac, Serbia (vranicaleksandra90@gmail.com)

[2]Center of Excellence for Redox Balance Research in Cardiovascular and Metabolic Disorders, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovica 69, 34000 Kragujevac, Serbia

[3]Department of Physiology, Faculty of Medical Sciences, University of Kragujevac, Svetozara Markovica 69, 34000 Kragujevac, Serbia

[4]I.M. Sechenov First Moscow State Medical University, Trubetskaya street 8, str. 2, 119991 Moscow, Russian Federation

[5]Department of Pharmacology of the Institute of Biodesign and Complex System Modelling, I.M. Sechenov First Moscow State Medical University, Trubetskaya street 8, str. 2, 119991 Moscow, Russian Federation

[6]Department of Human Pathology, First Moscow State Medical University I.M. Sechenov, Trubetskaya street 8, str. 2, 119991 Moscow, Russian Federation

Introduction

Metabolic syndrome (MetS) can be defined as a disorder including several entities such as insulin resistance, hyperglycemia, hypertension, hyperlipidemia and abdominal obesity according to the WHO (Saklayen, 2018). Over 30 million of people age > 18 have DM2 whereby prevalence of MetS is estimated to be at least three times higher (Smith, 2009). Therapeutic options for MetS management involve changes in lifestyle and the use of antidiabetic and antihyperlipidemic drugs. An alternative medicine approach is also gaining popularity due to several advantages, with significantly fewer side effects being the most important one (Pérez-Martínez, 2017). According to this, more attention has been focused on dietary supplements, nutraceuticals and functional foods used to mitigate hyperglycemia and prevent the development of MetS (Xu, 2018).

Members of the genus *Trametes*, encompassing approximately 60 different species, are highly appreciated species within the mentioned context. *Trametes versicolor (L.) Lloyd*, aka *Coriolus versicolor* or turkey tail mushroom, has been the most thoroughly investigated *Trametes* species so far (Meng, 2022). The *in vitro* antioxidant, anti-inflammatory and antimicrobial effects of T. versicolor have also been reported but there is a lack of data regarding the antidiabetic hypolipidemic properties of this mushroom and its polysaccharides (Bains, 2020).

According to the previous mentioned, we assumed that a 4-week supplementation of TV heteropolysaccharides (TVH) will influence redox status, especially in rats with metabolic syndrome.

Materials and methods

Total of forty healthy male *Wistar albino* rats (six weeks old, body-weight 200 ± 30 g) were included in this study. The animals were fed with standard rat diet (9% fat, 20% protein, 53% starch and 5% fiber), tap water *ad libitum* and housed under controlled regular environmental conditions.

The experimental design was performed in the Center of preclinical and functional research, Faculty of Medical Sciences, University of Kragujevac, Serbia in accordance with the current ethical norms approved by the Ethics Committee of the Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia, number: 06/17.

After a one-week environment adaptation, MetS was induced by feeding the rats with high-fat diet (HFD—25% fat, 15% protein, 51% starch and 5% fiber) for 4 weeks followed by a single intraperitoneal injection of streptozotocin (STZ) in a dose of 25 mg/kg (Abdel-Hamid, 2019). MetS was confirmed by measuring fasting glucose and insulin levels, lipid status and blood pressure 72 h post-streptozotocin injection and the animals with fasting blood glucose.

All rats were divided into the five groups: CTRL (n = 8)—untreated healthy animals fed with standard diet; MetS (n = 8)—untreated rats with induced MetS; H-TV (n = 8)—rats treated with 300 mg/kg (high dose of TV); M-TV (n = 8)—rats treated with 200 mg/kg (medium dose of TV); L-TV (n = 8)—rats treated with 100 mg/kg (low dose of TV). Groups of animals with induced MetS were fed with HFD till the end of the study. TVH was administered per os at the appropriate dose every day at the same time for four weeks.

All animals were sacrificed, and blood samples were collected from jugular vein to evaluate the systemic redox state. Blood samples were centrifuged in order to separate the plasma and red blood cells, which were stored at −20 °C until biochemical analysis. The following pro-oxidant parameters were determined from plasma samples: hydrogen peroxide (H_2O_2), superoxide anion radical (O_2^-), nitrites (NO_2^-), and index of lipid peroxidation (TBARS). Parameters of the antioxidative defense system were determined from erythrocyte lysate samples: the activity of superoxide dismutase (SOD) and catalase (CAT) and the level of reduced glutathione (GSH) as previously described (Jeremic, 2018).

Results and discussion

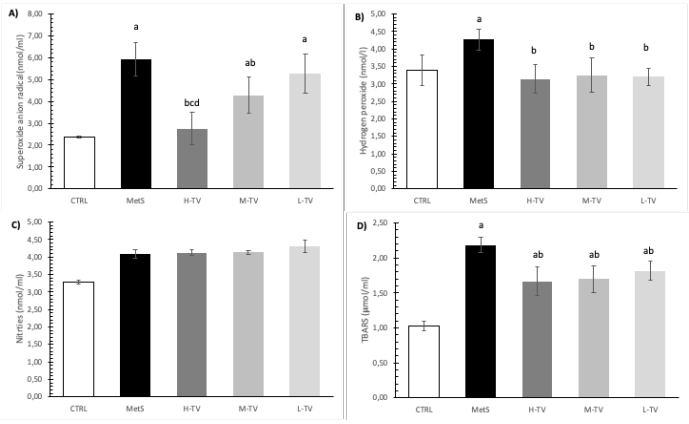
The induction of MetS led to a significant increase in the release of prooxidants, O_2^-, H_2O_2 and TBARS, compared to healthy CTRL rats ($p < 0.05$). The treatment with TVH significantly decreased the release of all measured prooxidant parameters, O_2^-, H_2O_2 and TBARS, except NO_2^-. The H-TV group had the most prominent effect on O_2^- compared to medium and low doses of TVH supplementation ($p < 0.05$).

The rats with MetS showed signs of highly compromised antioxidant systems; their levels of SOD, CAT and GSH were significantly lower than in control group of healthy individuals ($p < 0.05$).

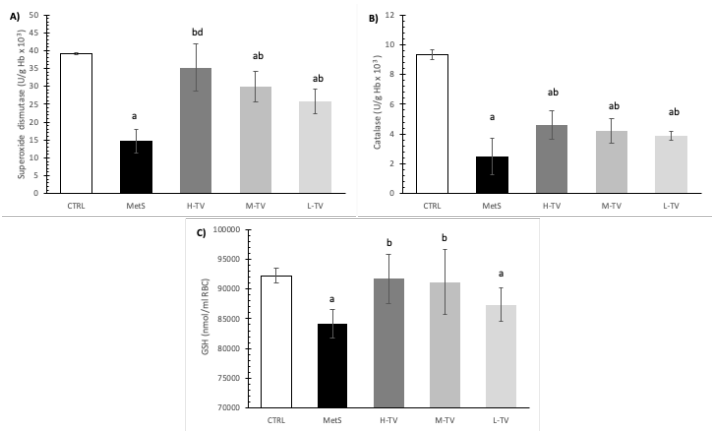
The four-week administration of TVH in all three investigated doses induced a significant increment of antioxidant enzymes activity (SOD and CAT) compared to the MetS rats. The increase in SOD activity in the H-TV group was

superior relative to the L-TV group ($p < 0.05$), while there were no significant differences in CAT activity between the three applied doses of TV ($p > 0.05$; Figure 3A,B).

These results correlate with previuos findings, suggesting that the amelioration of oxidative stress by TVH in MetS conditions may also originate from polysaccharopeptides, besides the phenolic acids and flavonoids mentioned (Lo, 2020).



Graph 1. Effects of TVH administration on antioxidant parameters. (A) Superoxide anion radical (O_2^-), (B) hydrogen peroxide (H_2O_2); (C) nitrites (NO_2^-); (D) index of lipid peroxidation (TBARS). CTRL: control group of healthy non-treated rats; MetS: control group of rats with induced metabolic syndrome; H-TV: rats with metabolic syndrome treated with high dose of T. versicolor; M-TV: rats with metabolic syndrome treated with medium dose of T. versicolor; L-TV: rats with metabolic syndrome treated with low dose of T. versicolor. Data are presented as means ± standard deviation. Statistical significance at the level $p < 0.05$: a compared to CTRL; b compared to MetS; c compared to HTV group; d compared to M-TV group.



Graph 2. Effects of TVH administration on antioxidant parameters. (A) Superoxide dismutase (SOD), (B) catalase (CAT) and (C) reduced glutathione (GSH). CTRL: control group of healthy nontreated rats; MetS: control group of rats with induced metabolic syndrome; H-TV: rats with metabolic syndrome treated with high dose of T. versicolor; M-TV: rats with metabolic syndrome treated with medium dose of T. versicolor; L-TV: rats with metabolic syndrome treated with low dose of T. versicolor. Data are presented as means ± standard deviation. Statistical significance at the level $p < 0.05$: a compared to CTRL; b compared to MetS; d compared to L-TV group.

Conclusion

H-TV and M-TV significantly reduced the level of prooxidants (O_2^-, H_2O_2, TBARS; $p < 0.05$), increased antioxidants activity (SOD, CAT, GSH; $p < 0.05$). The obtained results demonstrated that the TVH may be considered a potentially useful agent for redox balance in MetS conditions.

References

Saklayen M.G. (2018). The Global Epidemic of the Metabolic Syndrome. Current hypertension reports. 20(2):12.

Smith S.C. Jr. (2009). International Diabetes Federation Task Force on Epidemiology and Prevention, National Heart, Lung, and Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society, International Association for the Study of Obesity Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and

Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 120:1640–1645.

Pérez-Martínez P., Mikhailidis D.P., Athyros V.G., Bullo M., Couture P., Covas M.I., de Koning, L., Delgado-Lista J., Díaz-López A., Drevon C.A. et al. (2017). Lifestyle recommendations for the prevention and management of metabolic syndrome: An international panel recommendation. Nutrition reviews. 75:307–326.

Xu L., Li Y., Dai Y., Peng J. (2018). Natural products for the treatment of type 2 diabetes mellitus: Pharmacology and mechanisms. Pharmacological research. 130:451–465.

Meng F., Lin, Y., Hu L., Feng,W., Su P., Wu L. (2022). The Therapeutic Effect of Coriolus versicolor Fruiting Body on STZ-Induced ICR Diabetic Mice. Journal of healthcare engineering. 2022, 7282453.

Bains A., Chawla P. (2020). In vitro bioactivity, antimicrobial and anti-inflammatory efficacy of modified solvent evaporation assisted Trametes versicolor extract. Biotech 2020, 10, 404.

Abdel-Hamid H.A., Abdalla M.M.I., Zenhom N.M., Ahmed R.F. (2019). The effect of peptide tyrosine tyrosine (PYY3-36), a selective Y2 receptor agonist on streptozotocin-induced diabetes in albino rats. Endocrine regulations. 53:26–33.

Jeremic J., Nikolic Turnic T., Zivkovic V., Jeremic N., Milosavljevic I., Srejovic, I., Obrenovic R., Jancic S., Rakocevic M., Matic S., et al. (2018). Vitamin B complex mitigates cardiac dysfunction in high-methionine diet-induced hyperhomocysteinemia. Clinical and experimental pharmacology & physiology. 45:683–693

Lo H.C., Hsu T.H., Lee C.H. (2020). Extracellular Polysaccharopeptides from Fermented Turkey Tail Medicinal Mushroom, Trametes versicolor (Agaricomycetes), Mitigate Oxidative Stress, Hyperglycemia, and Hyperlipidemia in Rats with Type 2 Diabetes Mellitus. International journal of medicinal mushrooms. 22: 417–429