

# Valorization of White Grape Pomace Waste: Effects of a Polyphenol-Rich Extract on Oxidative Stress and Lipid Profile in Diet-Induced Dyslipidemic Rats

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**Introduction:** Valorization of grape pomace (GP) waste represents an important strategy for addressing both environmental and economic challenges associated with the wine industry. By transforming this abundant by-product into valuable products, GP valorization contributes to reducing environmental pollution while promoting resource efficiency within a circular economy framework (Fontana *et al* (2013); Karastergiou *et al* (2024)). Among winery residues, white grape pomace (WGP), composed mainly of skins, seeds, and stems remaining after juice extraction, is particularly rich in polyphenols, flavonoids, and other bioactive compounds. These constituents have been widely reported to exert antioxidant, anti-inflammatory, antimicrobial, anticancer, and metabolic health-promoting effects, highlighting the potential of WGP as a functional ingredient for health-related applications (Karastergiou *et al* (2024); Baroi *et al* (2024); Pop *et al* (2025)). In this context, the present study aimed to investigate the effects of WGP extract administration on oxidative stress parameters and lipid metabolism, specifically total cholesterol and triglyceride levels, in a rat model of diet-induced dyslipidemia.

**Materials and methods:** Forty adult male Wistar rats (200–250 g) were used in the study and maintained under controlled laboratory conditions (22 ± 2 °C, 50–60% humidity, 12 h light/dark cycle) with free access to food and water. After one week of acclimatization, animals were randomly divided into five experimental groups (n = 8 rats per group): ND, receiving a normal diet; HFD, receiving a hyperlipidic diet to induce dyslipidemia; HFD + RSV, receiving a hyperlipidic diet and rosuvastatin (ROSU) (10 mg/kg body weight/day); HFD + GP1, receiving a hyperlipidic diet and WGP extract equivalent to 400 mg polyphenols/kg body weight/day; and HFD + GP2, receiving a hyperlipidic diet and WGP extract equivalent to 200 mg polyphenols/kg body weight/day. Dyslipidemia was induced by administering the hyperlipidic diet for 30 days, while treatments were given daily by oral gavage throughout the experimental period. At the end of the study, blood samples were collected, serum was separated by centrifugation, and stored at –80 °C until analysis. Total cholesterol and triglycerides were determined using enzymatic colorimetric methods, while oxidative stress markers, including malondialdehyde (MDA), total oxidative status (TOS), nitric oxide (NO), total antioxidant capacity (TAC), total thiols, and oxidative stress index (OSI) were assessed using spectrophotometric assays. Results were expressed as mean ± standard deviation, and statistical differences between groups were evaluated using one-way ANOVA followed by Bonferroni post hoc test, with p < 0.05 considered statistically significant.

**Results:** Induction of dyslipidemia through the hyperlipidic diet resulted in significant alterations in lipid metabolism (Fig. 1A) and oxidative status (Fig. 1B).

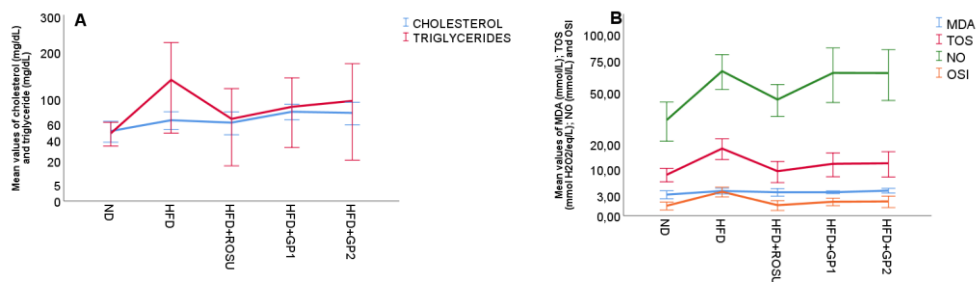


Figure 1. Serum concentration of cholesterol and triglycerides (A) and malondialdehyde (MDA), Total Oxidative Stress (TOS), nitric oxide (NO), and oxidative stress index (OSI) in rats fed with a hyperlipidic diet. Animals were grouped in ND (Normal Diet group), HFD (High-Fat Diet group), HFD + ROSU (HFD + rosuvastatin), HFD + GP1 (HFD + white grape pomace extract equivalent to 400 mg polyphenols/kg body weight/day) and HFD + GP2 (HFD + white grape pomace extract equivalent to 200 mg polyphenols/kg body weight/day).

Total cholesterol levels were significantly higher in the HFD group compared with the ND group ( $p = 0.006$ ), confirming the successful induction of dyslipidemia. However, no significant reduction in cholesterol levels was observed in the HFD+ROSU or HFD+GP2 groups when compared with the HFD group ( $p > 0.05$ ). In contrast, the HFD+GP1 group showed significantly higher cholesterol values compared with the HFD group ( $p = 0.023$ ). Further, triglyceride levels were markedly increased in the HFD group compared with the ND group ( $p < 0.001$ ).

Treatment with rosuvastatin significantly reduced triglyceride levels compared with the HFD group ( $p = 0.0025$ ), while the reductions observed in the GP1 ( $p=0.051$ ) and GP2 groups did not reach statistical significance, although a decreasing trend was noted. Induction of dyslipidemia was also associated with increased oxidative stress, as reflected by malondialdehyde (MDA) levels (Fig. 1B). The HFD group exhibited significantly higher MDA values compared with the ND group ( $p = 0.001$ ), confirming enhanced lipid peroxidation following high-fat feeding. A similar significant difference was observed between the ND group and the HFD+GP2 group ( $p < 0.001$ ). In contrast, comparisons between ND and HFD+ROSU as well as ND and HFD+GP1 were not statistically significant ( $p > 0.05$ ), although both groups showed intermediate values. Total oxidative status (TOS) was significantly higher in the HFD group compared with the ND group ( $p < 0.001$ ). Administration of rosuvastatin and WGP extracts significantly reduced TOS levels compared with the HFD group ( $p < 0.001$ ). In parallel, total antioxidant capacity (TAC) was significantly increased in the HFD+ROSU, HFD+GP1, and HFD+GP2 groups compared with the HFD group ( $p < 0.005$ ), indicating improved antioxidant defense. Consequently, the oxidative stress index (OSI) was significantly reduced in the treatment groups compared with the HFD group, reflecting an overall improvement in the oxidative balance. In addition, thiol levels were significantly higher in the HFD+GP2 group as compared with the HFD group ( $p < 0.001$ ), suggesting enhanced restoration of redox homeostasis following administration of the lower dose of grape pomace extract.

**Discussions:** Administration of WGP in rat models has been shown to exert beneficial effects on oxidative stress and dyslipidemia. In a type 2 diabetes model, dietary supplementation with 10% WGP flour improved fasting glucose, reduced serum triglycerides and cholesterol, and ameliorated oxidative damage in the liver, as well as protected pancreatic  $\beta$ -cells from streptozotocin-induced injury (Piccoli *et al* (2024)). The antioxidant capacity and bioavailability of phenolic acids from WGP were dose-dependent, with increased plasma antioxidant activity observed following oral administration in Wistar rats (Gerardi *et al* (2020)). Regarding dyslipidemia, diets containing up to 20.7% GP led to decreased blood triglyceride and very low-density lipoprotein (VLDL) levels, while high-density lipoprotein (HDL) and low-density lipoprotein (LDL) increased slightly, with total cholesterol remaining constant (Smith *et al* (2017), Yu *et al* (2017)). Thus, the results reported here are consistent with the ones in the literature data, administration of WGP extract demonstrating significant antioxidant and redox-modulating effects in diet-induced dyslipidemia, although its hypolipidemic activity was less pronounced than that of rosuvastatin.

**Conclusions:** These findings support the potential of waste GP valorization as a sustainable source of bioactive compounds with antioxidant activity, capable of mitigating oxidative stress associated with dyslipidemia, although its lipid-lowering effect appears limited compared with rosuvastatin under the present experimental conditions.

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