ABSTRACT

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Training Workplace	Department of Biochemical Sciences
Doctoral Degree Program	Xenobiochemistry and Pathobiochemistry
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Title of Doctoral Thesis	Detoxification enzymes in the pathogenesis of metabolic dysfunction-associated steatotic liver disease

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease, affecting approximately one-third of the population, and thus represents a significant global health concern. The prevalence of this disease is rising in parallel with the pandemic of obesity, metabolic syndrome, and type 2 diabetes mellitus. MASLD is characterized as a range of liver abnormalities, beginning with benign intrahepatic lipid accumulation (steatosis), that might further progress to more severe forms of the disease, including steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma. Given the significant structural and pathophysiological changes in the liver caused by MASLD, alterations in the expression and activity of key hepatic detoxification enzymes involved in the organism's antioxidant defense and drug metabolism may occur.

In the liver of murine in vivo models of MASLD, a diet rich in fat, fructose, and cholesterol (FFC) and/or the administration of monosodium glutamate (MSG) resulted in significant increase in the catalytic activity of superoxide dismutase, catalase, glutathione peroxidase, carbonyl reductase 1, and NAD(P)H:quinone oxidoreductase 1. Conversely, the administration of MSG alone led to a marked decrease in the catalytic activity of glutathione S-transferase and cytochrome P450 1A1/2, as well as a significant increase in the expression of miR-29b-3p, miR-200a-3p, and miR-200b-3p within the scope of epigenetic regulation.

While the bioinformatic prediction of miR-29b-3p binding complementarity with the 3' untranslated region of the glutathione peroxidase 7 transcript was confirmed in in vitro cell models, the predicted regulation of this transcript by miR-335-5p was not experimentally validated.

These findings contribute to a deeper understanding of changes in detoxification enzymes and epigenetic regulators in the context of MASLD and underscore the complexity of this disease.