The impact of novel lipid-lowering drugs on the expression of inflammatory markers in Triton WR 1339 induced hyperlipidemic rats

By

Yasmeen Mahmoud Sudqi "Zaid al-Kilani"

Supervisor

Dr. Suhair Hikmat

Co-supervisor

Prof. Lama Hamadneh

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Abstract

Hyperlipidemia is related to chronic inflammation, which may cause the emergence of cardiovascular issues like atherosclerosis, strokes and heart attacks. Atherosclerosis is a disorder in which gradual plaque buildup within the arteries leads to hardening and narrowing of these arteries. Thus, leads to blood flow limitation and increased risk of critical diseases. Hyperlipidemia is correlated with inflammation, as seen with increased expression of different inflammatory markers such as C-reactive protein, tumor-necrosis factor-alpha, interleukins and chemokines. The goal of this study was to investigate the correlation between novel anti-hyperlipidemic compounds and the expression of specific inflammatory markers in Triton WR 1339 induced hyperlipidemic rats. Male rats were

categorized to six groups: a normal control group, a hyperlipidemic control group, four hyperlipidemic groups administrated with fenofibrate, NF4BP, NF3BP and NF4AP respectively. After 20 hours of treatment, the rats were sacrificed, and the expression of specific inflammatory markers were assessed using real-time PCR. Fold changes in *CRP, TNF-a, IL-38, CXCL16, IL-1 β, IL-6, VCAM-1,* and *ICAM-1* were measured after administration of the novel compounds. Our results illustrated that the novel compounds significantly lower total triglycerides levels in comparison to the hyperlipidemic control group. Moreover, the results revealed a significant downregulation of *CRP, with a fold change of* (-3.2174), *IL-1β* (-7.3434), *IL-6* (-4.8919), and *ICAM-1* after administration with NF4AP; the findings also showed a significant downregulation of *TNF-a* (-4.4299) and *IL-1β* (-5.9983) after administration with NF3BP; and there was also a significant downregulation of *IL-1β* expression (-5.8748) after administration with NF4BP, suggesting a substantial suppression of pro-inflammatory signaling. It is noteworthy that the expression of anti-inflammatory IL-38 was overexpressed with a fold change of (42.1876) after administration of NF4BP. On the other hand, there was no significant effect of novel compounds on the expression of *VCAM-1.* As well as, the gene expression of *CXCL16* was significant downregulated after administered with the novel compounds. In conclusion, understanding the impact of novel anti-hyperlipidemic compounds on inflammatory marker expression is critical for developing effective therapeutic strategies for managing hyperlipidemia-associated complications. By targeting these inflammatory pathways, these compounds may offer new avenues for the prevention of dyslipidemia complications. However, the potential implications of the observed overexpression of *IL-38* should be considered, due to its anti-inflammatory properties, *IL-38* may aid in

reducing the inflammatory processes that contribute to the emergence and progression of hyperlipidemia by inhibiting the inflammatory response.

Keywords: Atherosclerosis, Hyperlipidemia, Inflammatory markers, Interleukins, Pro-inflammatory cytokines.