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Letter to the Editor

Trans fat-induced metabolic and endothelial injury: A convergent pathway accelerating atherogenesis

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Dear Editor,

Despite substantial progress in global food policy, recent analyses demonstrate that industrial trans fatty acids (TFAs) remain detectable in a wide range of commercially prepared foods, including baked goods, confectionery products, frying oils, and fast-food items [1]. Even though overall population exposure has declined in many regions, residual intake persists and may still be sufficient to exert biologically relevant effects. Accumulating evidence indicates that TFAs may act through dual, interconnected pathways—metabolic dysregulation and vascular injury—that collectively may contribute to atherogenesis beyond lipid profile changes alone.

From a metabolic perspective, TFAs have been reported to influence hepatic lipid handling. They have been associated with increased de novo lipogenesis, impaired β-oxidation, and worsening hepatic insulin resistance, potentially contributing to the development and progression of non-alcoholic fatty liver disease (NAFLD) [2, 3]. NAFLD in turn may promotes increased very-low-density lipoprotein (VLDL) secretion, elevating circulating low-density lipoprotein (LDL) concentrations [4]. Importantly, hepatic steatosis and systemic inflammation may enhance oxidative stress, potentially rendering LDL particles more susceptible to oxidative modification—a critical step driving macrophage lipid uptake and foam cell formation [4, 5].

It has also been noted that TFAs may be associated with an increase in visceral fat accumulation independently of total calorie load [6]. Visceral adipose tissue behaves as an active endocrine organ, releasing pro-inflammatory cytokines, adipokines, and free fatty acids. These mediators may aggravate systemic inflammation, intensify insulin resistance, and impose additional stress on the vascular endothelium, thereby fostering a metabolic environment permissive to atherosclerotic progression [6, 7].

Concurrently, TFAs have been associated with markers of vascular dysfuntion. They may impair endothelial nitric oxide (NO) bioavailability, increase reactive oxygen species, and activate NF-κB–dependent inflammatory cascades. These changes can promote monocyte recruitment and increase endothelial permeability by upregulating adhesion molecules such as VCAM-1, ICAM-1, and E-selectin; these are important early stages of atherogenesis [7, 8]. As LDL particles—already elevated and rendered more oxidation-prone by metabolic dysregulation—enter this inflammatory subendothelial compartment, they undergo rapid conversion into oxidized LDL (oxLDL).

OxLDL may promote macrophage recruitment and uptake via scavenger receptors, facilitating the formation of foam cells, a hallmark of early atherosclerotic lesions [8, 9]. ABCA1 and ABCG1 are key transporters mediating macrophage cholesterol efflux and reverse cholesterol transport, processes critically involved in limiting foam cell formation and atherogenesis [9]. While direct human evidence linking TFAs to modulation of these transporters remains limited, disturbances in lipid metabolism and inflammatory signaling associated with TFA exposure may have implications for macrophage cholesterol handling. These mechanisms may facilitate the transition from fatty streaks to more advanced, rupture-prone plaques.

Recent mechanistic studies suggest that individuals with NAFLD, metabolic syndrome, diabetes, or pre-existing endothelial dysfunction may exhibit heightened vascular susceptibility to oxLDL-driven foam cell formation and plaque progression [10]. As

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the prevalence of these conditions rises globally, the synergistic toxicity of TFAs across metabolic and vascular pathways becomes increasingly concerning. The integration of molecular, metabolic, and vascular evidence underscores that TFAs should be regarded not only as dyslipidemic nutrients but as potent accelerators of atherogenesis through multiple reinforcing mechanisms.

Given this convergent model—whereby TFAs elevate and oxidize LDL, promote hepatic steatosis, increase visceral obesity, impair endothelial function, and accelerate foam cell formation—it is imperative to adopt a more prevention-oriented framework. Even minimal residual exposure may be sufficient to activate these atherogenic processes. Thus, regulatory strategies should extend beyond simple manufacturing restrictions to include rigorous surveillance of imported and commercially prepared foods. Improved labeling practices, mandatory trans fat disclosure, and random market sampling may further safeguard the food environment.

Clinically, greater emphasis is needed on dietary counselling. Patients—especially those with NAFLD, obesity, diabetes, or established cardiovascular disease—should be explicitly advised to avoid all sources of trans fats. Positioning TFAs as preventable cardiovascular risk factors may improve adherence and help reduce long-term morbidity.

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