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Dimethyl Fumarate's Potential in Methanol Toxicity: A Critical Perspective on Future Research Directions

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Dear Editor,

After reading the study by Akyuz Unsal et al. (1) investigating the effects of dimethyl fumarate (DMF) on methanol (MeOH) toxicity, we would like to address an important gap in this research area. As the authors noted, the effects of DMF on organ-level MeOH toxicity have not been previously investigated, particularly considering the significant retinal side effects.

MeOH poisoning causes oxidative stress and retinal ganglion cell damage through its formic acid metabolite. DMF's proven antioxidant and anti-inflammatory properties in multiple sclerosis and psoriasis treatment may provide protective effects against these toxic processes (2). Indeed, DMF activates the *Nrf2* pathway, increasing antioxidant gene expression while suppressing pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha (3).

Although the study results were unexpected, the demonstration of DMF's safety profile is valuable. However, its potential for retinal protection could not be fully evaluated. Literature reports show that DMF exhibits protective effects in age-related macular degeneration, uveitis, and light-induced photoreceptor loss (4). These findings suggest DMF's therapeutic potential against MeOH's retinal toxicity.

The study's limitations, particularly the failure to establish a toxicity model, may have masked DMF's true effects. Future studies should include specific ophthalmological evaluations such as optical coherence tomography, electroretinography, and retinal ganglion cell counting. Additionally, testing different DMF doses and administration timing would be critical for determining optimal protective protocols.

Given the limited treatment options for MeOH poisoning, investigating multi-target agents like DMF is of great importance. Particularly, DMF's dual action of reducing oxidative stress and suppressing inflammation offers an ideal protective profile against MeOH's bidirectional toxic mechanisms (5).

This investigation represents a valuable foundation for exploring DMF's therapeutic potential in MeOH toxicity, despite methodological challenges encountered. Future research employing more sophisticated toxicity models and comprehensive retinal assessments could provide crucial insights that may ultimately translate into clinical therapeutic strategies for this life-threatening condition (6).

Sincerely,

Footnotes

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