Investigation of the Protective Effects of Natural Compounds Sodium Butyrate and Dihydromyricetin on Chronic Alcohol-Induced Brain Damage

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Presentation Outline

- Introduction to Alcohol-Induced Brain Damage
- Addressing Critical Therapeutic Gap
- Dihydromyricetin (DHM) - A Naturally Derived Neuroprotective Candidate
- Sodium Butyrate (SB) - An Endogenously Occuring Beneficial Short-Chain Fatty Acid
- Experimental Design and Results
- Conclusions
- Limitations and Future Directions

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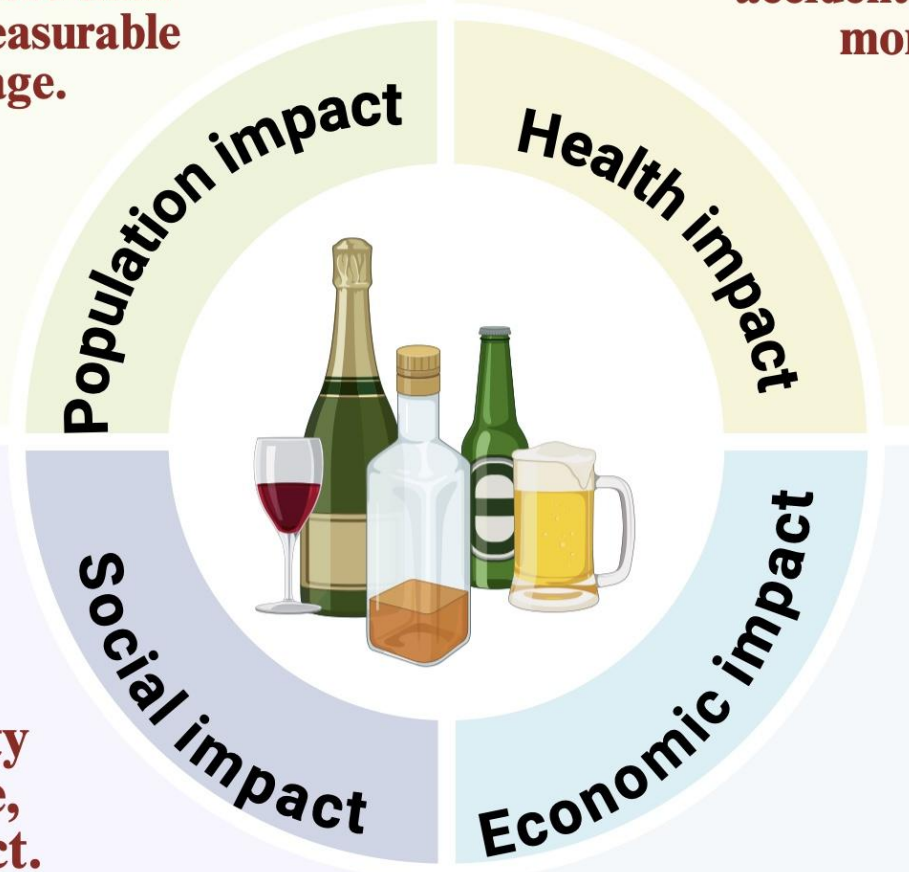
The Problem of Alcohol Use Disorder (AUD)

Over 16 million Americans are affected by AUD — with more than 80% showing measurable brain damage.

AUD increases the risk of liver disease, cancers, accidents, and early mortality.



AUD strains relationships, parenting, and community safety through violence, crime, and neglect.

Alcohol-related problems create billions in healthcare, productivity, and social-cost burdens.

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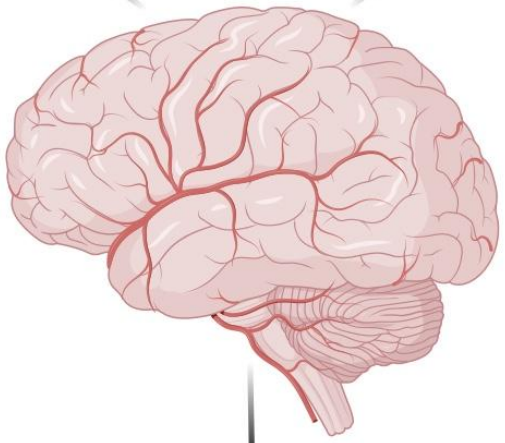
Alcohol-Induced Brain Damage: Key Molecular Pathways

Neuroinflammation
Microglia activation, Neuroinflammatory markers activation (IL-6,TNF-a)

Oxidative Stress
ROS generation, antioxidant depletion, lipid peroxidation



BBB Disruption
Tight junction loss and barrier leakiness

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AUD Treatment Options

There are three FDA approved pharmacotherapies for AUD:

- Acamprosate
- Disulfiram
- Naltrexone

However, none address the molecular pathways associated with alcohol-induced brain damage.

Goal: Target neuroinflammation, oxidative stress, and blood-brain barrier dysregulation to address alcohol-associated brain damage

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Dihydromyricetin

Ampelopsis grossedentata (Chinese Vine Tea)

Therapeutic Benefits

- Exhibits antioxidant and anti-inflammatory properties across multiple organ systems.
- Used in TCM as an anti-hangover remedy, and has been demonstrated to enhance alcohol metabolism and reduce liver injury.
- Formulated DHM (DHM-TEA) significantly improves solubility and enables effective oral administration.

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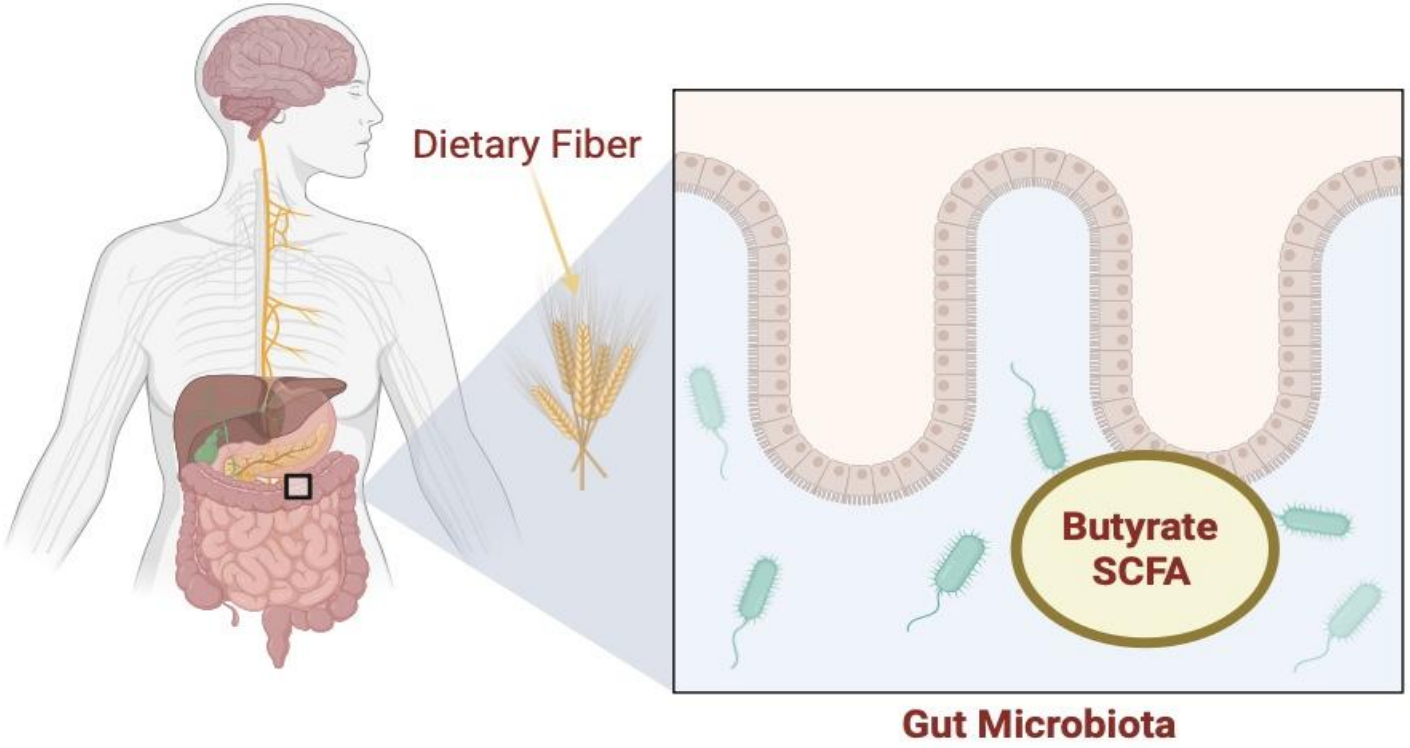
Butyrate



- Short-chain fatty acid (SCFA) produced by gut bacteria during fiber fermentation
- Energy source for enterocytes
- Preserves intestinal barrier
- Anti-inflammatory; HDAC inhibitor activity
- Readily available to tissues

Experimental Design

Male C57BL/6 mice

Experimental Groups

Control	Water	DHM-TEA (150 mg/kg)	SaB (300 mg/kg)
EtOH	EtOH	DHM-TEA+ EtOH	SaB+EtOH

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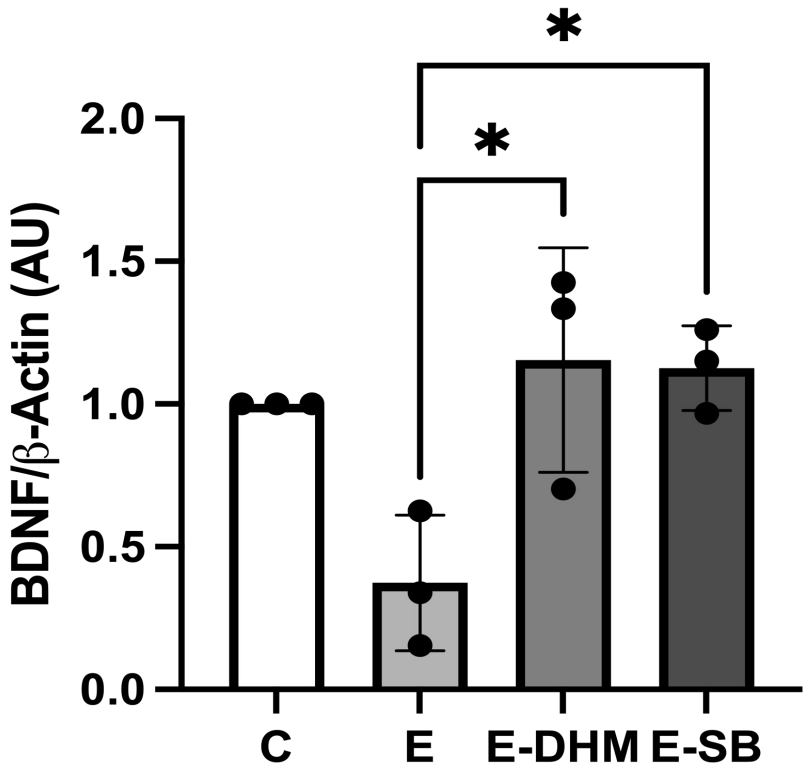
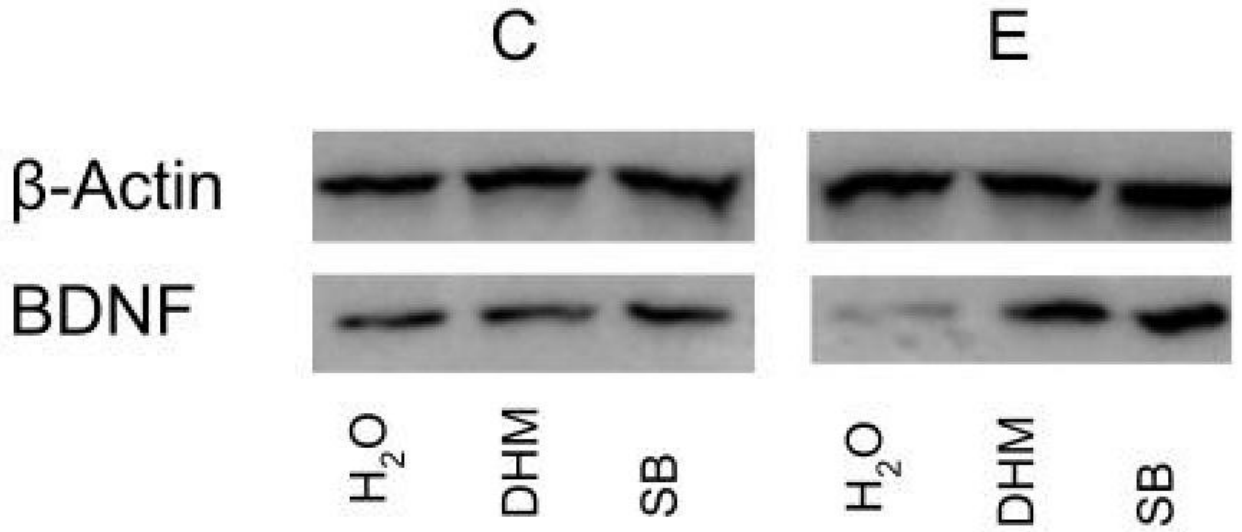
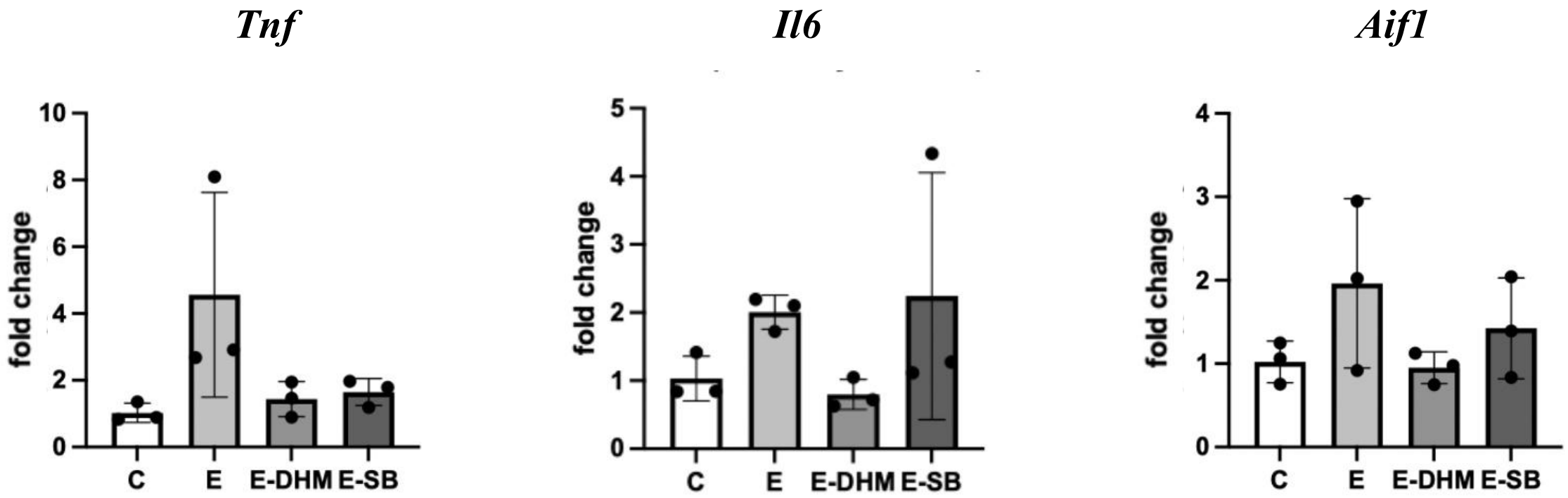
Effects of Treatments on Neuroplasticity Marker





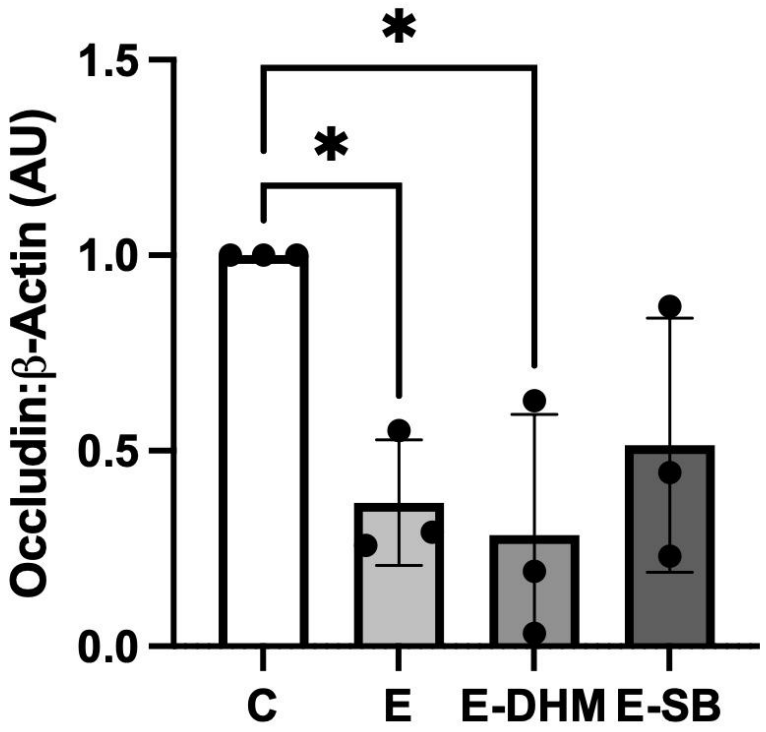
- Alcohol-induced BDNF reduction was restored by both DHM and SB treatments
- Suggests neurotrophic support

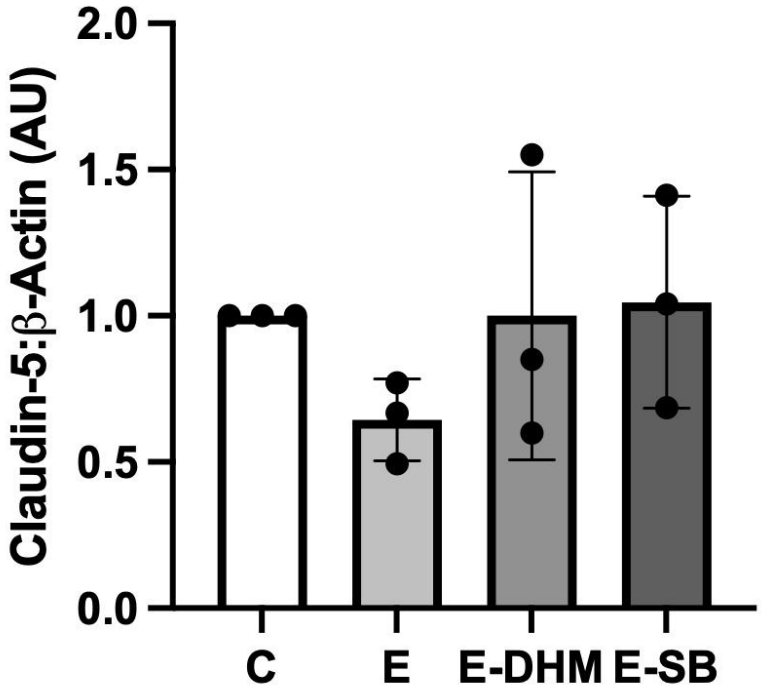
Effect of Treatments on Neuroinflammatory Markers

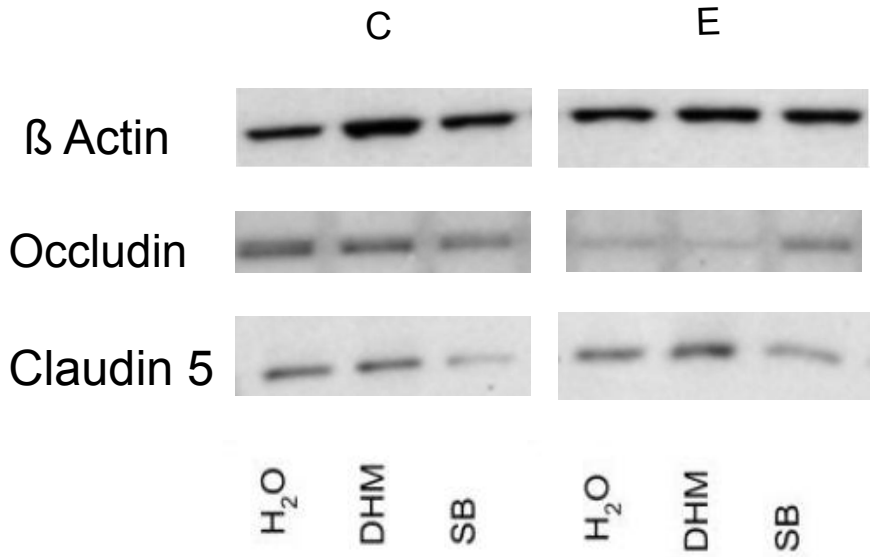


- Alcohol-induced increases in TNF-α, IL-6 and Iba-1 gene expression were restored by DHM
- SB treatment reduced TNF-α but not IL-6 and Iba-1 gene expression levels
- Note: Changes not significant

Effect of Treatment on Tight Junction Markers







- Alcohol decreased levels of Occludin and Claudin-5
- No significant effects of treatments were found

Conclusions

- Chronic alcohol exposure damages the brain through multiple connected mechanisms.
- DHM and sodium butyrate may protect the brain through complementary pathways.
- These compounds represent a promising foundation for future neuroprotective strategies.

Limitations

- The study exclusively used male C57BL/6 mice, limiting the generalizability of findings across sexes given known sex differences in alcohol metabolism and neurological responses.

- The 10-day Lieber-DeCarli model represents a relatively acute chronic exposure window and may not fully recapitulate the long-term neurological consequences of years of heavy alcohol consumption in humans.

- DHM's critically low oral bioavailability of approximately 4% and poor water solubility remain significant translational barriers, even with the TEA co-crystal formulation used in this study.

- Future investigations will address current methodological constraints while expanding our research scope into the broader physiological and behavioral dimensions of Alcohol Use Disorder.

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