

Effects of Perinatal Exposure to Diisononyl Cyclohexane-1,2-Dicarboxylate (DINCH) on the Development of Metabolic Dysfunction-Associated Steatotic Liver Disease in Male and Female Mice



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SCIENTIFIC RATIONALE

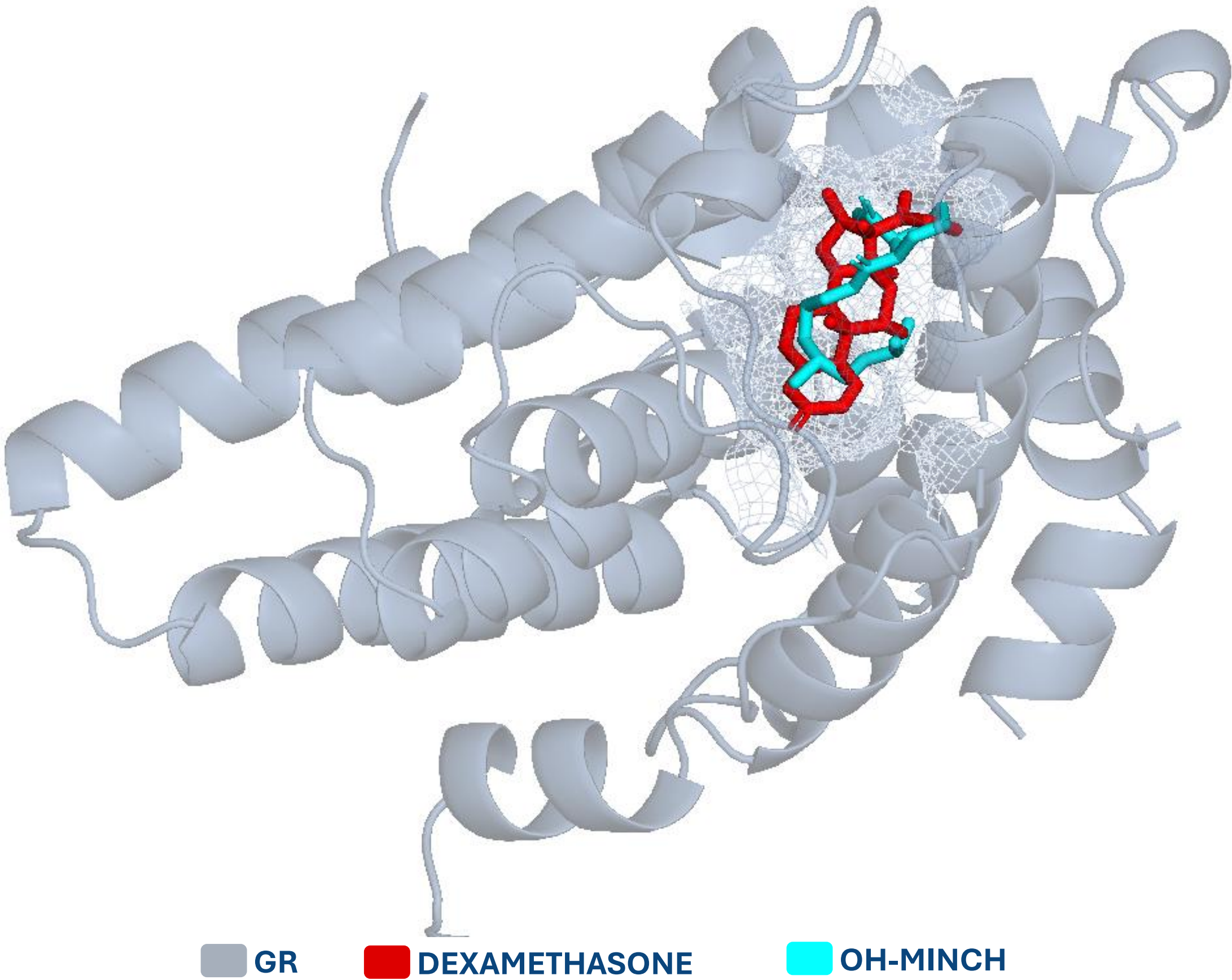
MASLD is the most prevalent chronic liver disease worldwide, affecting approximately one-third of the global population. Besides obesity and dietary factors, increasing evidence suggests that endocrine-disrupting chemicals (EDCs) contribute to disease development by disrupting metabolic homeostasis.

Diisononyl cyclohexane-1,2-dicarboxylate (DINCH) is an increasingly used phthalate substitute. Despite widespread human exposure, little is known about its long-term metabolic effects following developmental exposure.

Recent studies indicate that **glucocorticoid receptor (GR)** signaling regulates hepatic lipid metabolism. However, whether DINCH or its metabolite **OH-MINCH** interferes with GR signaling during early-life exposure remains unknown.

This study investigates whether perinatal DINCH exposure increases susceptibility to MASLD through disruption of GR signaling in a sex-dependent manner.

PRELIMINARY *IN SILICO* RESULTS

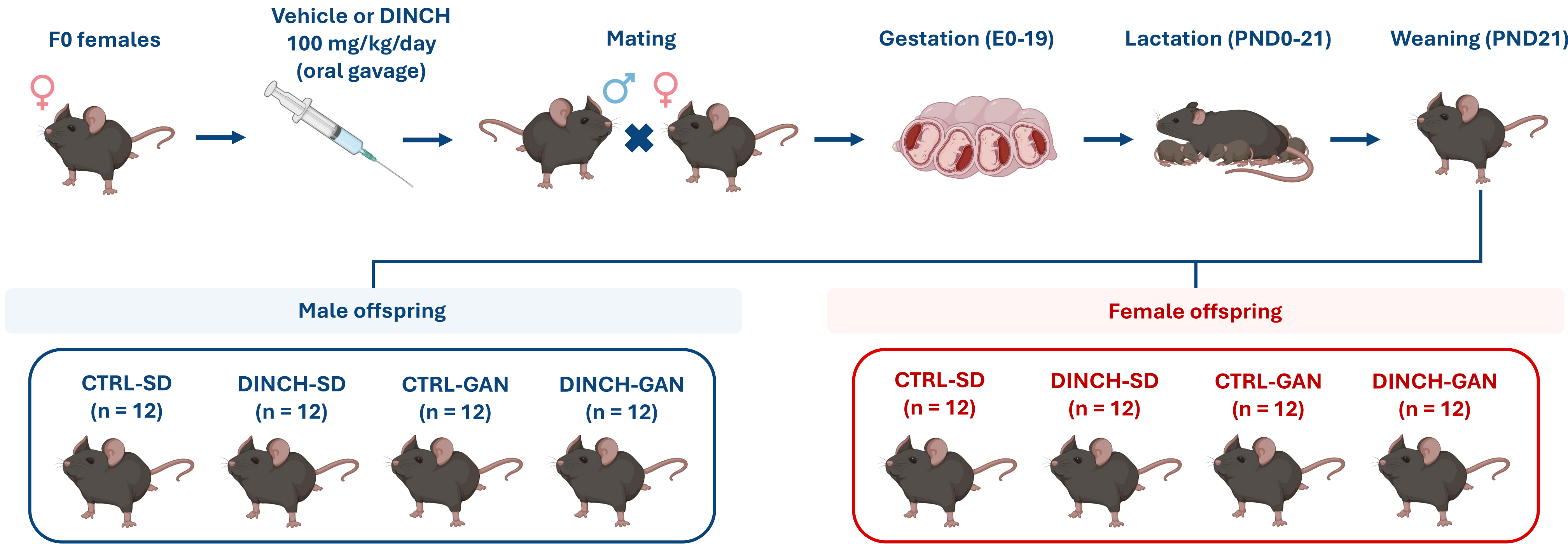


BINDING AFFINITY	
DEX	-12.62
OH-MINCH	-7.83
DINCH	-6.87

KEY FINDINGS

- OH-MINCH** occupies the canonical **GR** ligand-binding pocket.
- Partial overlap with **DEX** suggests shared interactions.
- OH-MINCH** may act as a weak modulator of **GR** signaling.

EXPERIMENTAL DESIGN



STUDY ENDPOINTS

Metabolic phenotype	Liver pathology	Glucocorticoid signaling	Molecular analyses
- Body weight - Food intake - GTT	- Serum ALT, AST, ALP - Liver histology (H&E, ORO)	- GR expression 11β-HSD1 - H6PDH - Serum corticosterone	- RT-qPCR - Western blot - Immunohistochemistry

EXPECTED OUTCOMES

We expect that this study will provide the first comprehensive evaluation of the effects of developmental DINCH exposure on susceptibility to metabolic dysfunction-associated steatotic liver disease (MASLD). Building on our preliminary molecular docking findings, the proposed *in vivo* study will determine whether glucocorticoid receptor signaling represents a mechanistic link between perinatal DINCH exposure and environmentally induced metabolic dysfunction. Furthermore, we expect to identify sex-dependent differences in metabolic responses, providing new insight into susceptibility to emerging plasticizers.