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VITAMIN E AND OXIDATIVE STRESS MODULATION IN THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE: CURRENT EVIDENCE AND CLINICAL PERSPECTIVES

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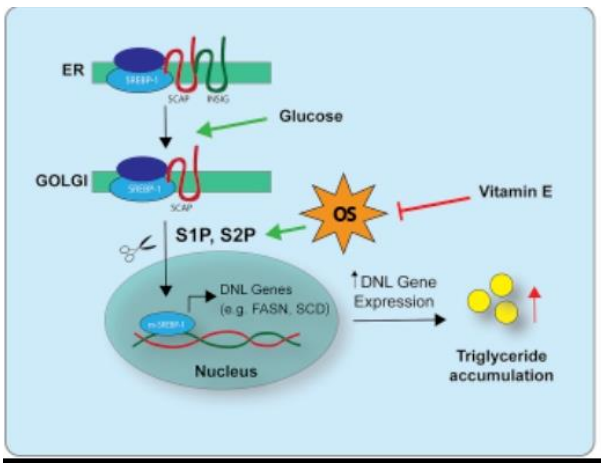
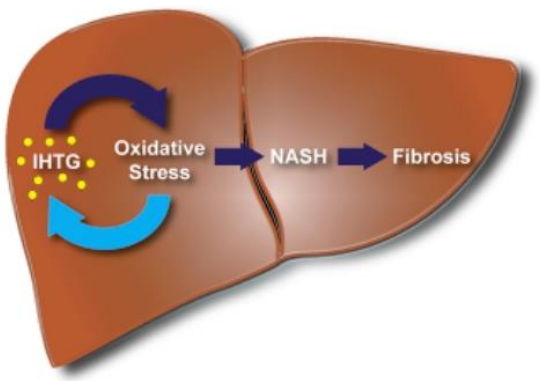
1. INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD), recently reclassified as metabolic dysfunction-associated steatotic liver disease (MASLD), encompasses a spectrum from simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma. It is strongly associated with metabolic syndrome, obesity, and insulin resistance.

Oxidative stress plays a pivotal role in disease progression. Vitamin E (α-tocopherol), a potent lipid-soluble antioxidant, has been extensively studied for its therapeutic role in reducing oxidative damage and improving liver histology in NAFLD.





2. Epidemiology
NAFLD affects approximately 25–30% of the global population and is increasingly prevalent in India due to urbanization and sedentary lifestyle patterns. NASH develops in about 10–20% of NAFLD patients and significantly increases morbidity and mortality.

3. Etiology and Risk Factors
NAFLD is a multifactorial disease with key contributing factors:
Insulin resistance
Obesity (central adiposity)
Type 2 diabetes mellitus
Dyslipidemia
High-calorie diet (fructose and saturated fats)
Genetic factors (e.g., PNPLA3 mutation)

4. Pathophysiology

NORMAL LIVER
↓
NAFLD (Fat accumulation)
↓
↑ Oxidative Stress
↓
NASH (Inflammation)
↓
Fibrosis (Scarring)
↓
Cirrhosis (Severe stage)

= Feedback Loop
Fat → ROS → More Fat accumulation

□ Vitamin E
Breaks oxidative stress cycle
Slows progression of disease

4.1 Multiple-Hit Hypothesis
NAFLD progression involves multiple parallel insults:
Hepatic fat accumulation
Lipotoxicity
Oxidative stress
Inflammatory cytokine release
Fibrogenesis

4.2 Role of Oxidative Stress
Reactive oxygen species (ROS) generated during fatty acid oxidation cause:
Lipid peroxidation
Mitochondrial dysfunction
Cellular injury and apoptosis
Oxidative stress is a key driver of transition from simple steatosis to NASH.

5. Role of Vitamin E in Oxidative Stress Modulation
Vitamin E acts as a chain-breaking antioxidant.
Neutralizes free radicals
Prevents lipid peroxidation
Stabilizes hepatocyte membranes
Reduces inflammatory mediators (TNF-α, IL-6)
Improves mitochondrial integrity

6. Clinical Features
Most patients are asymptomatic. Symptomatic individuals may present with:
Fatigue
Right upper quadrant discomfort
Hepatomegaly
Advanced disease may show features of cirrhosis and portal hypertension.

7. Diagnosis
Laboratory Tests
Elevated ALT and AST
Dyslipidemia
Insulin resistance
Imaging
Ultrasound (first-line)
MRI/CT
FibroScan
Gold Standard
Liver biopsy for diagnosing NASH and fibrosis staging

8. Management
8.1 Lifestyle Modification
Weight loss (7–10%)
Mediterranean diet
Regular exercise
8.2 Pharmacological Therapy
No definitive drug therapy exists; however, vitamin E is widely used in selected patients.

9. Vitamin E in NAFLD: Current Evidence
9.1 Clinical Trials
The PIVENS trial demonstrated that vitamin E significantly improved histological features in non-diabetic adults with NASH.

9.2 Biochemical Effects
Reduction in ALT and AST levels
Decrease in oxidative stress markers

9.3 Histological Effects
Improvement in steatosis and inflammation
Limited impact on fibrosis

9.4 Preventive Role
Higher dietary vitamin E intake correlates with reduced NAFLD risk.

10. Clinical Perspectives
Indications
Non-diabetic adults with biopsy-proven NASH
Dosage
400–800 IU/day α-tocopherol
Limitations
Inconsistent response
Minimal effect on fibrosis
Safety Concerns
Increased risk of hemorrhagic stroke

Possible association with prostate cancer
Combination Therapy
Emerging data supports combination with omega-3 fatty acids and insulin sensitizers.

11. Recent Updates
Recent meta-analyses confirm improvement in liver enzymes and histology.
MASLD terminology introduced to reflect metabolic etiology.
Research ongoing on combination therapies and personalized medicine.

12. CONCLUSION
Vitamin E plays a crucial role in modulating oxidative stress in NAFLD and shows significant benefits in improving biochemical and histological outcomes, particularly in NASH patients. However, limitations in fibrosis improvement and long-term safety concerns necessitate careful patient selection. Lifestyle modification remains the cornerstone of therapy, with vitamin E as an adjunct in selected individuals.

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