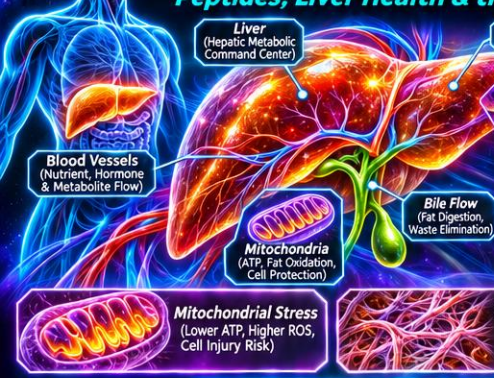
Peptide Perspectives™

BEYOND DETOX

Peptides, Liver Health & the Science of Cellular Protection

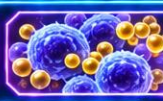


LIVER HEALTH IS ABOUT PROTECTION, NOT A 'CLEANSE'

- The liver is a metabolic command center, not just a filter.
- It stores and releases glucose, processes fats, makes proteins, produces bile, and transforms chemicals.
- MASLD and MASH are different from viral hepatitis, alcohol-related liver disease, autoimmune hepatitis, and cirrhosis from other causes.
- Limiting injury, identifying disease early, and supporting liver-cell resilience matter more than "detox" claims.

Mitochondrial Stress (Lower ATP, Higher ROS, Cell Injury Risk)

Fibrosis / Scarring (Extracellular Matrix Buildup, Stiffness, Reduced Function)



Nutrient Handling (Glucose, Fatty Acids, Triglycerides, and Lipid Export)

FOUR KEY BIOLOGICAL PATHWAYS

METABOLIC SWITCHBOARD



- Glucose handling (uptake, storage, and release).
- Glycogen storage and mobilization.
- Insulin resistance and its impact on liver fat.
- Liver fat (steatosis) and metabolic overload.

DRUG PROCESSING & BILE



- Phase I enzymes (e.g., CYP450) modify many drugs and chemicals.
- Phase II conjugation (e.g., glucuronidation, sulfation) helps make them more water-soluble.
- Bile production and flow support fat digestion and waste elimination.
- No peptide is proven to universally improve medication processing.

MITOCHONDRIA & OXIDATIVE STRESS



- ATP (cellular energy) production drives liver metabolism.
- Fatty-acid oxidation helps clear excess fat from the liver.
- Reactive oxygen species (ROS) can cause cellular stress and injury.
- MOTS-c and SS-31 are of interest for mitochondrial protection and stress resilience.

INFLAMMATION & FIBROSIS



- Kupffer cells (liver immune cells) can drive inflammatory signaling.
- Stellate cells can be activated (e.g., by TGF-beta) to produce scar tissue (fibrosis).
- Ongoing inflammation and fibrosis can reduce liver function and increase risk.
- The liver can regenerate, but this capacity is limited, especially with ongoing injury.

8 COMPOUNDS / STRATEGIES & THEIR EVIDENCE

1. SEMAGLUTIDE



- **Mechanism:** GLP-1–based metabolic therapy (↑ insulin, ↓ appetite, weight loss, improved liver metabolism).
- **Liver focus:** MASH with liver fat, inflammation, and fibrosis.
- **Evidence:** Phase 3 biopsy evidence in MASH; FDA-approved (Wegovy®) for defined noncirrhotic MASH with Fa⁻–F3 fibrosis.
- ⚠ **Key limitation:** Not for all liver disease (e.g., viral, autoimmune, or advanced cirrhosis).

2. TIRZEPATIDE



- **Mechanism:** Dual GIP/GLP-1 agonist (improves metabolic control, weight, and liver fat).
- **Liver focus:** MASH and metabolic liver disease (MASLD/MASH).
- **Evidence:** Phase 2 biopsy evidence showing MASH resolution signals (e.g., more frequent resolution vs. placebo).
- ⚠ **Key limitation:** Not U.S.-approved specifically for MASH.

3. MOTS-c



- **Mechanism:** Mitochondrial-derived peptide (modulates energy metabolism, stress response, and cellular resilience).
- **Liver focus:** Steatosis, inflammation, and fibrosis (preclinical interest).
- **Evidence:** Preclinical studies show potential liver protection (less fat, inflammation, and fibrosis).
- ⚠ **Key limitation:** No proven human liver efficacy.

4. SS-31 (ELAMIPRETIDE)



- **Mechanism:** Binds cardiolipin to stabilize mitochondrial membranes (↓ mitochondrial stress, ↑ efficiency).
- **Liver focus:** Protection from liver injury (e.g., steatosis, inflammatory, or toxic injury).
- **Evidence:** Preclinical studies show mitochondrial and liver-injury protection (e.g., less inflanmation and cell damage).
- ⚠ **Key limitation:** Approved pharmaceutical use in Barth syndrome does not equal liver approval.

5. OVAGEN (EDL)



- **Mechanism:** Liver-focused short-peptide bioregulator idea (proposed to support hepatocyte function and tissue repair).
- **Liver focus:** Liver-cell protection, metabolic balance, and regeneration (hypothetical).
- **Evidence:** Intriguing hypothesis and early research interest, limited and preliminary data.
- ⚠ **Key limitation:** No reliable human liver validation.

6. SURVODUTIDE



- **Mechanism:** GLP-1 plus glucagon agonist (combines metabolic and liver-targeted effects via weight loss and increased energy expenditure).
- **Liver focus:** Investigational therapy for MASH / MASLD (liver fat and inflammation).
- **Evidence:** Clinical studies show metactions in liver fat on MRI and favorable liver biomarkers; biopsy signals are being studied.
- ⚠ **Key limitation:** MRI liver-fat changes and biopsy outcomes are different and not interchangeable.

7. EFRUXIFERMIN



- **Mechanism:** FGF21 analogue (improves lipid metabolism, insulin sensitivity, and liver fat handling).
- **Liver focus:** Investigational strategy for liver fibrosis and broader liver-metabolic health.
- **Evidence:** Encouraging clinical trials (e.g., reductions in liver fat, inflammation, and fibrosis markers), but not approved.
- ⚠ **Key limitation:** Still investigational; long-term effects and approval are pending.

8. RESMETIROM



- **Mechanism:** Non-peptide THR-beta agonist (liver-selective thyroid hormone receptor-beta activation to reduce liver fat and fibrosis).
- **Liver focus:** MASH with fibrosis (F2–F3).
- **Evidence:** FDA-approved (Rezdiffra®) for noncirrhotic MASH with F2–F3 fibrosis (biopsy-confirmed).
- ⚠ **Key limitation:** Not a peptide; included as an important comparison benchmark.

THESE ARE DIFFERENT OUTCOMES

- **Lower ALT / AST** (reduced liver enzyme levels).
- **Less liver fat on MRI** (reduced hepatic fat content).
- **Less inflammation on biopsy** (less liver-cell inflammatory activity).
- **Fibrosis improvement** (less scarring / lower fibrosis stage).
- **Prevention of liver failure / major complications** (reduced risk of cirrhosis, decompensation, transplant, or liver-related death).

NOT INTER-CHANGEABLE

WHAT GOOD STUDIES SHOULD MEASURE

- Liver-biopsy endpoints when appropriate (e.g., MASH resolution, fibrosis stage).
- MRI liver fat and elastography (e.g., PDFF, liver stiffness).
- Fibrosis scores and liver function markers (e.g., ALT, AST, ALP, bilirubin, albumin, INR).
- Symptoms, quality of life, and metabolic health (e.g., weight, glycemic control, cardiometabolic risk).
- Long-term liver outcomes and safety (e.g., progression to cirrhosis, decompensation, and adverse events).

WHERE SCIENCE IS HEADING

- Better tissue-level outcome measurement (e.g., histology, advanced imaging, and molecular markers).
- Combination metabolic strategies (e.g., multi-agonist therapies and complementary approaches).
- Mitochondrial and cell-protection research (e.g., MOTS-c, SS-31, and related pathways).
- Distinguishing indirect metabolic benefit from direct liver effects (e.g., weight loss vs. liver-specific action).
- Earlier detection and stage-specific treatment (e.g., risk stratification and targeted therapy by disease stage).

⚠ LOWER ENZYMES, LESS FAT, LESS INFLAMMATION, AND LESS FIBROSIS ARE DIFFERENT OUTCOMES. EXPERIMENTAL PEPTIDES ARE NOT PROVEN LIVER 'DETOX' TREATMENTS.

Educational research overview | November 2026 | Not medical advice