

Based on the provided sources, several herbs and synergistic combinations can "reprogram" the liver to prevent ammonia buildup. This is achieved primarily by upregulating genes and enzymes associated with the urea cycle (which converts ammonia to urea), regulating glutamine metabolism, or modulating the gut-liver axis.

## Herbs that Upregulate Urea Cycle Enzymes

The following herbs appear to "reprogram" the liver by directly increasing the expression or activity of enzymes required to detoxify ammonia:

- **Naringin (Citrus Flavonoid):** This bioflavonoid, found in grapefruit and other citrus fruits, significantly upregulates the expression of key urea cycle enzymes, including carbamoyl phosphate synthase I (CPS I), ornithine transcarbamylase (OTC), argininosuccinate synthase (ASS), argininosuccinate lyase (ASL), and arginase I (ARG) 1. By modulating these proteins, naringin significantly augments the liver's capacity to remove ammonia from the blood 1, 2.
- **Fisetin:** This flavonoid exhibits chronotherapeutic potential (maximum effect observed when administered at 00:00 h). It increases the expression of critical liver enzymes—CPS-I, OTC, and ASS—as well as brain glutamine synthetase (GS), thereby reducing ammonia levels in hyperammonemic rats 3.
- **Yinchen Wuling Powder (YCWLPP):** This traditional Chinese medicine prescription was found to treat hepatic fibrosis by reprogramming nitrogen metabolism. Specifically, it increases the expression of **carbonic anhydrase 2 (CA2)** and **carbamoyl-phosphate synthetase 1 (CPS1)**, facilitating the conversion of ammonia into urea 4, 5.
- **Green Tea Catechins (GTCs):** Ingesting GTCs combined with exercise has been shown to improve endurance by enhancing the expression of urea cycle-related genes in the liver, which helps suppress ammonia accumulation 6.
- **Conclevan (Liver Hydrolysate):** While a hydrolysis product rather than a simple herb, it increases the mRNA expression levels of hepatic urea cycle enzymes (CPS, ASS, and arginase) and glutamine synthesis enzymes, effectively inhibiting blood ammonia accumulation 7.

## Synergistic Combinations and Formulas

Certain combinations work synergistically to modulate metabolic pathways or reduce toxicity:

- **Gallic Acid + Metformin:** The co-administration of gallic acid and metformin potentiates antioxidant and anti-inflammatory effects. This combination significantly reduces serum ammonia levels and improves liver function markers (ALT, AST, ALP) more effectively than monotherapy in models of acute hepatic encephalopathy 8, 9.
- **Dioscorea bulbifera L. (RDB) + Glycyrrhiza uralensis (Licorice):** Concocting the potentially hepatotoxic herb *Dioscorea bulbifera* with *Glycyrrhiza uralensis* juice reduces toxic components (like diosbulbin B) and alleviates liver injury. This combination lowers serum ammonia and transaminase levels while downregulating inflammatory pathways (NF-κB/COX-2) 10, 11.

- **Antrodia camphorata + Panax ginseng:** This synergistic formulation reduces serum ammonia, lactate, and blood urea nitrogen (BUN) levels in dose-dependent manners, aiding in fatigue recovery and liver metabolic function 12, 13.
- **Babao Dan (BBD) + Lactulose:** In clinical settings, combining the traditional medicine BBD with lactulose significantly reduced blood ammonia levels and improved neurocognitive function in patients with minimal hepatic encephalopathy compared to lactulose alone 14.
- **Xiaoyao San (XYS):** This formula regulates glutamine and glutamate metabolic pathways in the liver to maintain ammonia balance and promote energy metabolism, serving as a link between hepatoprotection and antidepressant effects 15, 16.

## Other Hepatoprotective Herbs Reducing Ammonia

Several other plant extracts have been identified to lower ammonia levels, often by mitigating oxidative stress or inflammation which compromises liver function:

- **Uncaria rhynchophylla:** This herb significantly reduces serum ammonia levels in acute liver injury models by suppressing oxidative stress (via myeloperoxidase) and inflammation (via NF-κB) 17.
- **Schefflera arboricola:** Methanol extract from the leaves of this plant returned ammonia levels to near normal in rats with thioacetamide-induced hepatic encephalopathy 18.
- **Resveratrol:** This polyphenol reduces circulating ammonia and restores neuronal tight junction proteins in cirrhotic models 19, 20. It also mediates antioxidant pathways (Nrf2/HO-1) to attenuate mitochondrial dysfunction induced by ammonia 21.
- **Allicin (from Garlic):** Oral administration of allicin restores serum liver functions and reduces hepatic and brain levels of ammonia in a dose-dependent manner 22.
- **Rubus coreanus:** Extracts from this fruit significantly lowered plasma ammonia levels in fatigue models compared to controls 23.
- **Schisandra (Schizandrin):** Significantly reduces elevated levels of ammonia and liver enzymes in mice with chronic liver injury 24.
- **Barnebydendron riedelii:** Flavonoids from this plant were shown to improve brain neurotransmitters and ammonia levels in a dose-dependent manner 25.

## Mechanisms of Action

These botanical agents prevent ammonia buildup through three primary mechanisms:

1. **Enzyme Induction:** Directly stimulating the transcription and activity of urea cycle enzymes (CPS1, OTC, ASS) to convert ammonia into urea 1, 4.
2. **Pathway Modulation:** Regulating the glutamine-glutamate cycle to facilitate ammonia detoxification in the liver and brain 6, 16.
3. **Cytoprotection:** Reducing oxidative stress and inflammation (e.g., via Nrf2/HO-1 pathways), which preserves hepatocyte function and prevents the secondary accumulation of ammonia caused by liver cell necrosis 26, 27.