

Based on the provided sources, the efficacy of herbs and plant-derived compounds for hearing disorders (including age-related hearing loss/presbycusis, noise-induced hearing loss, and tinnitus) can be ordered by the strength of the evidence presented, ranging from human clinical trials and meta-analyses to preclinical animal models.

## 1. Ginkgo Biloba

*Evidence Level: High Volume of Human Research (Mixed/Controversial Results)*

Ginkgo biloba is the most extensively studied herbal remedy in the provided sources, though results are conflicting depending on the specific condition and extract used.

- **Sudden Hearing Loss:** A meta-analysis of 27 randomized controlled trials involving 2,623 patients found that adjuvant therapy with *Ginkgo biloba* extract (GBE) was superior to general treatments alone in improving total effective rates and pure tone hearing thresholds in patients with sudden sensorineural hearing loss 1.
- **Tinnitus:** The standardized extract **EGb 761** has shown efficacy in treating tinnitus, particularly in patients where tinnitus is a primary complaint or associated with dementia 2. However, a Cochrane systematic review concluded that evidence for *Ginkgo biloba* in treating tinnitus is very uncertain, suggesting little to no effect on symptom severity compared to placebo 3, 4.
- **Presbycusis (Age-Related Hearing Loss):** Clinical trials have produced negative results. One study found no benefit from *Ginkgo biloba* extract (120 mg/day) on tinnitus or hearing thresholds in elderly patients after six months of therapy 5, 6.

## 2. Panax Ginseng (and Ginsenosides)

*Evidence Level: Human Trials and Strong Animal Models*

Ginseng and its active components (ginsenosides) show consistent protective effects across different types of hearing loss in both human and animal studies.

- **Noise-Induced Hearing Loss (NIHL):** In a human study involving workers exposed to noise, the group receiving Ginseng (200 mg/day) showed better distortion product otoacoustic emission (DPOAE) amplitudes than the control group, though less effective than N-acetyl-cysteine (NAC) 7, 8.
- **Age-Related Hearing Loss:** In animal models, Korean Red Ginseng (KRG) delayed the progression of age-related hearing loss and improved auditory function, potentially by inhibiting senescence-related genes 9, 10.
- **Cellular Protection:** Ginsenoside Rc was shown to promote cell survival and alleviate inflammation and apoptosis in cochlear cells injured by palmitate 11.

## 3. Traditional Chinese Medicine (TCM) Formulas

*Evidence Level: Strong Preclinical (Animal) Evidence and Network Pharmacology*

Several specific TCM decoctions have been validated in animal models for their ability to delay age-related hearing loss (ARHL).

- **Erlong Zuoci Decoction (ELZCD):** This formula significantly reduced hearing threshold elevation and protected spiral ganglion cells and mitochondria in aged C57BL/6J mice

12, 13. Network pharmacology predicts it modulates apoptosis and inflammatory responses 14, 15.

- **Yi-Qi Cong-Ming (YQCM):** This decoction was found to restore cell viability and mitochondrial membrane potential in oxidative stress models, modulating apoptosis in auditory hair cells 16.
- **Jian Er (JEJ):** In a mouse model, this TCM preparation reduced apoptosis, protected cochlear sensorineural cells, and significantly delayed the progression of age-related hearing loss 17, 18.

#### 4. Resveratrol (Stilbenoids)

*Evidence Level: Strong Preclinical Evidence*

Resveratrol, a polyphenol found in grapes and red wine, is repeatedly highlighted for its otoprotective properties against various insults.

- **Age-Related Hearing Loss:** Long-term supplementation with resveratrol reduced age-related cochlear hair cell loss, spiral ganglion neuron loss, and vascular atrophy in mice 19. It was found effective in preventing ARHL, particularly when treatment started *prior* to the onset of hearing loss (early treatment) 20, 21.
- **Noise and Ototoxicity:** Resveratrol has been identified as an otoprotective agent against noise trauma and drug-induced ototoxicity 22.
- **Mechanisms:** It activates the **SIRT1** pathway, which regulates mitochondrial biogenesis and autophagy to protect cochlear cells 19, 23.

#### 5. Pueraria lobata (Kudzu) / Puerarin

*Evidence Level: Preclinical Evidence*

- **Age-Related Hearing Loss:** Treatment with *Pueraria* significantly improved hearing thresholds and hemorheological items (blood flow properties) in aged rats, with an optimal dosage identified at 2 g/kg 24. It acts as a vasodilator and may improve cochlear microcirculation 25.

#### 6. Thymoquinone (Nigella sativa)

*Evidence Level: Systematic Review of Preclinical Studies*

- **Acquired Hearing Loss:** A systematic review highlighted *Nigella sativa* and its active compound, thymoquinone, as promising candidates for preventing acquired sensorineural hearing loss, particularly ototoxicity, due to antioxidant and anti-apoptotic properties 26, 27.
- **Age-Related Hearing Loss:** High-dose thymoquinone significantly improved auditory sensitivity and reduced apoptosis in aged mice 28.

#### 7. Emerging Phytochemicals (Single Studies)

The following plant-derived compounds have shown efficacy in specific animal or *in vitro* models but appear less frequently in the provided text than those above:

- **C-Phycocyanin (Spirulina):** Attenuated noise-induced cochlear synaptopathy and inflammation in guinea pigs 29.
- **Astragaloside IV (Astragalus):** Reduced hearing thresholds and inflammatory factors in mice exposed to noise, potentially by regulating intestinal flora 30, 31.
- **Celastrol (Tripterygium wilfordii):** Identified as a potential compound for treating diseases via ferroptosis pathways, though the specific context in the source was hepatocellular carcinoma, it is listed among TCM agents for hearing loss 32, 33.
- **Castanopsis echinocarpa:** Showed protective effects against neomycin and noise-induced hearing loss in zebrafish and mice 34.
- **Silymarin (Milk Thistle):** Doses of 100 and 200 mg/kg prevented significant auditory brainstem response threshold shifts in a D-galactose-induced aging rat model 35.

## Summary Table of Efficacy

Herb / Compound, Primary Indication, Evidence Strength in Sources, Mechanism

Ginkgo Biloba, "Tinnitus, Sudden HL", Mixed Human Data (Positive for sudden HL/specific extract; Negative for presbycusis), "Antioxidant, blood flow improvement"

Ginseng (KRG), "NIHL, Presbycusis", Positive Human & Animal Data, "Anti-apoptotic, mitochondrial protection"

"TCM Formulas (Erlong Zuoci, etc.)", Presbycusis, Strong Animal Data, "Multitarget: Anti-apoptosis, mitochondrial regulation"

Resveratrol, "Presbycusis, NIHL", Strong Animal Data, "SIRT1 activation, mitochondrial biogenesis"

Pueraria, Presbycusis, Positive Animal Data, "Vasodilation, microcirculation improvement"

Thymoquinone, "Ototoxicity, Presbycusis", Positive Animal Data, "Antioxidant, anti-inflammatory"