Tinnitus Medical Treatment

- Case Report: Potential of pharmacological treatment for auditory abnormal sensations with aripiprazole: a report of two cases
- Recent advances on the mechanism of acupuncture in the treatment of subjective tinnitus
- A Position Statement on the Treatment of Hearing Impairment, Focused on Hearing Aids, From the Korean Otological Society Hearing Aid Study Group
- Effectiveness and tolerability of liraglutide as add-on treatment in patients with obesity and high-frequency or chronic migraine: A prospective pilot study
- Objective assessment of tinnitus laterality
- When the Mind Meets the Ear: A Scoping Review on Tinnitus and Clinically Measured Psychiatric Comorbidities
- Hearing Improvement after Radiation Therapy for a Facial Nerve Schwannoma: Report of a Case and Review of Literature
- Chronic tinnitus is quietened by sound therapy using a novel cross-frequency de-correlating stimulus modulation

Medical treatment for tinnitus aims to reduce perception, alleviate associated symptoms (anxiety, insomnia, depression), and improve quality of life. No medication has been proven to eliminate tinnitus, but several agents may be used off-label in selected cases.

Antidepressants

Tricyclic Antidepressants (TCAs)

- **Examples:** Amitriptyline, Nortriptyline
- **Mechanism:** Inhibit serotonin and norepinephrine reuptake; sedative and anticholinergic effects
- **Indications:** Tinnitus with comorbid depression, anxiety, or insomnia
- **Caution:** Anticholinergic side effects (dry mouth, cognitive slowing); cardiotoxicity in overdose

Selective Serotonin Reuptake Inhibitors (SSRIs)

- **Examples:** Paroxetine, Sertraline
- **Role:** May help reduce distress in patients with anxiety or depression
- **Evidence:** Mixed; not proven to reduce tinnitus loudness
- **Adverse effects:** Sexual dysfunction, GI symptoms, withdrawal syndrome

Benzodiazepines

- **Examples:** Clonazepam, Diazepam
- **Mechanism:** GABA-A receptor agonists → sedation, anxiolysis
- **Use:** Short-term relief in severe tinnitus-related anxiety or insomnia
- **Risks:** Dependence, tolerance, cognitive impairment, falls in elderly

Anticonvulsants

- **Examples:** Gabapentin, Carbamazepine, Topiramate
- **Rationale:** Modulate neural hyperexcitability
- **Evidence:** Limited and inconsistent
- **Adverse effects:** Sedation, dizziness, mood changes

Anxiolytics / Hypnotics

- **Melatonin:** May improve sleep quality and reduce perception in some patients
- **Hydroxyzine:** Antihistamine with anxiolytic effects; sometimes used for nocturnal symptoms

Other Medications

NMDA Antagonists

- **Example:** Memantine
- **Mechanism:** Inhibits glutamatergic excitotoxicity
- **Status:** Experimental; limited clinical benefit

Calcium Channel Blockers

- **Example:** Verapamil
- **Use:** Theoretical benefit in vascular tinnitus; minimal evidence

Ginkgo Biloba (Herbal)

- **Mechanism:** Vasoactive and antioxidant properties
- **Evidence:** Contradictory; not superior to placebo in most trials
- **Use with caution:** May increase bleeding risk

Summary Table

Drug Class	Examples	Target	Comment
Antidepressants	Amitriptyline, Paroxetine	Mood, distress	May reduce emotional impact
Benzodiazepines	Clonazepam	Anxiety, insomnia	Use short-term only
Anticonvulsants	Gabapentin, Topiramate	Neural excitability	Off-label use
Hypnotics	Melatonin	Sleep	Well-tolerated adjunct
Vascular agents	Verapamil	Vascular regulation	Experimental
Herbal	Ginkgo Biloba	Circulation, stress	Inconclusive evidence

Limitations

- No drug currently **cures** tinnitus
- Most treatments are **off-label** and based on small studies
- Focus should be on **individualized symptom control**

Randomized double-blind placebo-controlled clinical trials

In a randomized, double-blind, placebo-controlled clinical trial, Lee et al. aimed to determine the optimal dosing strategies for two pharmacological combinations in tinnitus [1)]

Major Weaknesses

⚠ 1. Sample Size Fallacy

- Nortriptyline–Topiramate Combination group: n = 19
- Verapamil–Paroxetine Combination group: n = 22
- → Far too small to support meaningful dose-response conclusions or subgroup analyses

⚠ 2. Descriptive Data Masquerading as Evidence

- No inferential statistics reported for dose comparisons
- No placebo-adjusted outcomes presented in this secondary analysis
- Authors infer “dose optimization” from trends that lack statistical significance

⚠ 3. Pharmacologic Oversight

- No rationale for combining drugs with overlapping toxicity (e.g., anticholinergic + cognitive + cardiovascular effects)
- No pharmacokinetic modeling, interaction studies, or tolerability stratification

⚠ 4. Misleading Framing with MCID

- ~41–42% reached Minimal Clinically Important Difference in both groups
- No clear placebo differential reported
- MCID is treated as a robust outcome without accounting for variability or regression to the mean

⚠ 5. Language Bias and Overinterpretation

- Claims such as “effective dosing” and “early responders required escalation” are not supported by statistical rigor
- Creates an illusion of clinical utility from exploratory data

Clinical Applicability

- No long-term follow-up
- No safety profile for chronic use of either combination
- No reproducibility due to small sample and lack of confirmatory trials
- No generalizability to real-world tinnitus subtypes

Conclusion

This study provides **no reliable evidence** to guide dosing of polypharmacy regimens in tinnitus. Its conclusions are based on **small samples, descriptive trends, and rhetorical inflation**. It is best viewed as a hypothesis-generating exercise — not a clinical recommendation.

Verdict:

- *High risk of misinterpretation*
- *Methodological rigor: Low*
- *Clinical usefulness: Negligible*

1)
Lee EJ, Tawk K, Gutiérrez Pérez ML, Tsang C, Abouzari M, Djalilian HR. Optimal Dosing of Nortriptyline-Topiramate and Verapamil-Paroxetine Combinations in Tinnitus Treatment. Laryngoscope. 2025 Jun 14. doi: 10.1002/lary.32338. Epub ahead of print. PMID: 40515518.