



Alternative medications and other treatments for tinnitus: facts from fiction

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Since the dawn of human existence, nutritional supplements, herbs, and phytonutrients have been used to heal. Forty percent of Americans have used some form of complementary-integrative medicine (CIM) to treat a wide variety of chronic conditions. In 1998, expenditures on CIM in the United States approached \$27 billion and increased to \$32 billion in 2000 [1]. This paradigm shift to alternative forms of therapy is gaining acceptance for many reasons including patients' dissatisfaction with conventional medical care, which is perceived to be too intent on curing rather than preventing disease, and the fact that prescription medicines have many side effects and hence, patients are often non-compliant. Conversely, the conventional western physician is typically skeptical of CIM practices because of the lack of double-blind randomized placebo-controlled studies. This is a particularly difficult problem because the pharmaceutical industry is not routinely interested in funding studies to assess the efficacy of herbs and other supplements because patent protection is unlikely. Coupled with the fact that the cost to bring a compound through the US Food and Drug Administration averages \$300 million or more, it is no wonder that studies into this arena are rare [2].

Conventional medical fields, such as allopathic and osteopathic medicine, were only introduced in the United States less than 200 years ago. This subsequently led to the rapid reduction in CIM therapies because these were suddenly viewed as antiquated and a form of quackery. The unfortunate result of this skepticism was the overemphasis solely on conventional medicine as a means to heal and cure. In the best scenario, tapping into knowledge from both CIM and conventional medicine would likely lead to better overall care of patients.

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The use of medication for treatment of tinnitus has largely been varied and anecdotal. Such drugs as nicotinic acid, carbamazepine, baclofen, and others have been tried and even tested in double-blind placebo-controlled trials (Table 1) [3]. Few have been shown to be significantly beneficial in adequately designed studies. Lidocaine has been studied in several carefully controlled double-blinded studies and shown to be beneficial. Lidocaine, however, must be given intravenously, has a very short half-life, and is often accompanied by undesirable side effects. Oral analogs of lidocaine, such as tocainide and flecainide acetate, did not improve tinnitus [4]. A double-blind, placebo-controlled study using melatonin (3 mg at bedtime) was found to have no advantage over placebo in relieving tinnitus. Among patients reporting difficulty sleeping attributable to their tinnitus, however, 46.7% reported an overall improvement after melatonin compared with 20% for placebo [4]. Benzodiazepines also may provide relief, especially for patients with concurrent depression. In one study, 76% of patients taking alprazolam had a reduction in the loudness of their tinnitus, whereas only 5% of the placebo group showed benefit [5]. Education, counseling, tinnitus retraining therapy, and medications remain the major modalities in the treatment of tinnitus. Many individuals have reported that these have provided either resolution of, or produced the greatest decrease in, their symptoms.

This article discusses treatment alternatives for chronic tinnitus. Examples include variations in diet, vitamin supplementation, herbal medicine, and other modalities. Although these options are considered alternative to many traditional physicians, it should be emphasized that there is currently no cure for tinnitus. The treatments discussed in this article have been beneficial for some people who have constant tinnitus, especially those whose tinnitus failed to respond to traditional treatment modalities. Altering one's diet has been shown to improve tinnitus in some patients. Many patients with tinnitus report that certain supplements seem to have a variable benefit in reducing their symptoms. Nutrient supplementation to treat tinnitus has been extensively studied. The following have generated the most interest and support: magnesium, calcium, potassium, lipoflavonoids, B vitamins, copper, selenium, zinc, and manganese. Herbal remedies for this ailment include *Ginkgo biloba*, black cohosh, mullein, and cornus. Other treatments, such as laser-light therapy, enzymatic therapy, tinnitus retraining, and vibrational therapy, are also discussed.

Vitamin B complex

The B-complex vitamins are a family of nutrients that have been grouped together because of the interrelationships in their function within human enzyme systems, and their distribution in natural food sources. Deficiency in these vitamins has been shown to result in tinnitus [6], and supplementation may improve the symptom. The B vitamins are water soluble and easily absorbed, except vitamin B₁₂, whose absorption is enhanced by intramus-

Table 1
Medications used to treat tinnitus

Anesthetics	Lidocaine/lignocaine (Xylocaine IV) Procaine (Novocain IV) Tocainide (Tonocard)-oral lidocaine analogue Flecainide acetate (Tambocor)
Antidepressants	Nortriptyline (Pamelor) Paroxetine (Paxil) Fluoxetine (Prozac) Sertraline (Zoloft) Bupropion (Wellbutrin) Amitriptyline (Elavil)
Anticonvulsants	Carbamezapine (Tegretol) Phenytoin (Dilantin) Primidone (Mysoline)
Anti-anxiety Agents	Alprazolam (Xanax) Clonazepam (Klonopin) Diazepam (Valium)
Antispastic	Baclofen (Lioresal)
Antihistamines	Chlorpheniramine (Chlor-Trimeton) Meclizine
Diuretics	Furosemide (Lasix)
Vasoactive medications	Histamine Hydergine Vinpocetine Pentoxifyline (Trental)
Herbs	Ginkgo biloba Black cohosh Ligustrum Mullein Pulsatilla St. John Wort
Vitamins and minerals	Magnesium (400 mg/d) Calcium (1000 mg/d) Potassium (2500 m/d) Zinc Manganese Copper Vitamin B ₁₂ Beta carotene Selenium Vitamin C Vitamin E Niacin

cular injection or sublingual application. Nevertheless, oral B₁₂ supplementation still leads to increased serum levels. Unlike fat-soluble nutrients, most B-complex vitamins cannot be stored in the body, and must be replaced daily from food sources or supplements.

The B vitamins function as coenzymes to facilitate human metabolism and energy production. They maintain healthy skin, eyes, muscle tone, and support the functions of the liver and central nervous system. They are also important in helping to deal with depression, stress, and anxiety. Normally, B vitamins are taken as a complex, but a single B vitamin may be indicated to treat a particular disorder. Deficiency in B vitamins may also result in lethargy, anemia, nervousness, skin and hair problems, decreased appetite, poor night vision, and hearing loss [7].

Vitamin B₁ (thiamine)

Vitamin B₁ (thiamine) is a nutrient with a critical role in maintaining a healthy central nervous system. Adequate thiamine levels can dramatically affect cognitive function by maintaining a positive mental attitude and enhancing learning abilities. Conversely, inadequate levels of B₁ can lead to vision problems, mental confusion, and loss of physical coordination.

Vitamin B₁ is required for the production of hydrochloric acid, forming blood cells, and for maintenance of healthy circulation. It also plays a key role in converting carbohydrates into energy, and in maintaining proper muscle tone of the digestive and cardiovascular systems. A chronic deficiency of thiamine leads to beriberi, a devastating and potentially deadly disease of the central nervous system. Beriberi is diagnosed clinically by peripheral neuropathy and cardiovascular and cerebral dysfunction, which includes congestive heart failure and dementia. Because of improved diets and the widespread use of supplements, beriberi is rare in developed countries, with one important exception. Beriberi symptoms are occasionally seen in chronic alcoholics because of the destructive effect alcohol has on B₁. Thiamine levels can also be affected by ingestion of antibiotics, sulfa drugs, caffeine, antacids, and oral contraceptives. A diet high in carbohydrates can also increase the need for B₁.

Food sources high in thiamine include beans, eggs, brewers yeast, whole grains, brown rice, and seafood. In supplemental form, B₁ is generally found in a combination with vitamins B₂, B₃, B₆, pantothenic acid, and folic acid. There are no known toxic effects from vitamin B₁, and any excess is excreted from the body. The recommended dietary intake (RDI) for B₁ is 1.5 mg, although more typical daily intake ranges from 50 to 500 mg/d [8].

Some patients have noted that vitamin B₁ supplements relieve their tinnitus [9]. The mechanism of action seems to be by a stabilization effect on the nervous system, especially in the inner ear. Dosages ranging from 25 to 500 mg/d have been used.

Vitamin B₃ (niacin)

Vitamin B₃ (also called niacin, niacinamide, or nicotinic acid) is an essential nutrient required for proper metabolism of carbohydrates, fats,

and proteins, and for the production of hydrochloric acid. Vitamin B₃ also supports circulation, healthy skin, and aids in the functioning of the central nervous system. Because of its role in supporting the higher functions of the brain and cognition, vitamin B₃ also plays an important role in the treatment of schizophrenia and other mental illnesses, and in stabilizing cognitive functions. Adequate levels of B₃ are vital for the proper synthesis of insulin, and the sex hormones, estrogen, testosterone, and progesterone. Natural food sources for vitamin B₃ include beef, broccoli, carrots, cheese, corn flour, eggs, fish, milk, potatoes, and tomatoes. Foods containing vitamin B₃, however, provide minimal amounts of this vitamin.

A deficiency in vitamin B₃ can result in pellagra, a disorder characterized by malfunctioning of the nervous system and gastrointestinal upset. Classically, the three cardinal symptoms are diarrhea, dementia, and dermatitis. Recently, niacin has been embraced by the medical community for its ability to safely lower cholesterol and triglyceride serum levels. The dosing required is between 500 and 2000 mg daily. Doses exceeding 1000 mg can lead to hepatotoxicity and are more common in the timed-release niacin supplements. When recommending doses in this range, liver function tests need to be monitored [8].

Niacin at any dose may result in a niacin flush, a natural reaction that is harmless but can be uncomfortable. A niacin flush generally results in a burning, tingling, and itching sensation, accompanied by a reddening flush that spreads across the skin of the face, arms, and chest, typically lasting 5 to 60 minutes [8]. A nonflush form of niacin now exists, which may be better tolerated by some patients, but this is the form that is more apt to cause potential liver problems.

There is no accepted standard niacin dosing for tinnitus. Typically, the senior author recommends beginning at 50 mg twice a day. After 2 weeks, if there is no improvement, the patient increases the dose by 50 mg at each interval to a maximum dose of 500 mg twice per day. Higher doses can be recommended, but it is advised to monitor liver function tests. Niacin may provoke migraine headache attacks in some people and appropriate warning is justified. High doses should be used with caution in pregnant women. Mega doses of pure niacin can aggravate health problems, such as stomach ulcers, gout, glaucoma, and diabetes mellitus.

Unfortunately, there is no clinical proof for the effectiveness of niacin in treating tinnitus. This is inherently difficult to prove because of a possible placebo effect arising from the niacin flush sensation rather than any therapeutic value of the underlying vasodilation. The senior author has noted a favorable response to niacin in some patients. There have been other anecdotal reports of the benefit of niacin in treating tinnitus [9].

Some health care providers advocate taking niacin in combination with thiamine. The 1994 text on myofascial pain, *Trigger Points*, states that niacin without thiamine seems to provide little relief for tinnitus [10]. This has not, however, been the senior author's experience. The combination dosing is

two parts niacinamide for each one part thiamine. Some supplements come balanced in this proportion.

There have also been reports of niacin working in combination with lecithin, a group of phospholipids that yield two fatty acid molecules and one molecule each of glycerophosphoric acid and choline after hydrolysis. Lecithin is found in nervous tissue, especially myelin sheaths, and in the plasma membrane of plant and animal cells. The theory is that the lecithin, being an emulsifier, helps disperse the buildup of fats in the capillaries, and the niacin helps dilate the capillaries to allow the lecithin in. The phosphatidylcholine portion of lecithin, however, is a precursor of acetylcholine and should be avoided in people who are manic-depressive because it may worsen the depressive phase. Compelling evidence exists from experiments in the authors' laboratory demonstrating that aged rats supplemented with a diet rich in phosphatidylcholine have improved auditory sensitivity when compared with placebo-supplemented rats. Furthermore, study of the subjects' mitochondrial function reveals a statistically significant improvement in mitochondrial energy production in the treated groups compared with placebo (Seidman et al, [11]).

Vitamin B₁₂

Vitamin B₁₂, also referred to as *cobalamin* and *cyanocobalamin*, is a micronutrient that is water soluble like other B vitamins. Unlike the other B vitamins, however, which are not stored in the body, vitamin B₁₂ is stored for up to 9 months in the liver and kidneys.

The RDI for vitamin B₁₂ is 2 µg for adults, 2.2 µg for pregnant women, and 2.6 µg for nursing mothers [12]. Vitamin B₁₂ is not found in vegetables, but can be found in pork, blue cheese, clams, eggs, herring, kidney, liver, seafood, and milk.

It has been estimated that 5% to 10% of persons over the age of 65 years are deficient in vitamin B₁₂. With newer and more sensitive tests available, deficiency states have been found in as many as 15% to 20% of the population [13]. This deficiency state is most likely secondary to absorption difficulties and a deficient nutritional intake. There may be some correlation between the decline in vitamin B₁₂ levels and the increasing prevalence of tinnitus in the elderly.

Vitamin B₁₂ is an important coenzyme required for the proper synthesis of DNA and new cell formation. It also works synergistically with vitamin C to aid in proper digestion and absorption of foods, protein synthesis, and the normal metabolism of carbohydrates and fats. Additionally, B₁₂ prevents nerve damage by contributing to the formation of the myelin sheath. Vitamin B₁₂ also maintains fertility, and helps promote normal growth and development in children.

Metabolites, including cobalamin, are involved in stabilizing neural activity. Vitamin B₁₂ is an essential cofactor for methylation of myelin basic

protein and cell membrane phospholipids. Cobalamin deficiency has been shown to be a factor involved in neuronal dysfunction. It is logical to assume that a relationship between tinnitus, which might involve neuronal dysfunction, and vitamin B₁₂ deficiency may exist. In the senior author's experience, several patients who were motivated to attempt nutritional supplementation with B₁₂ noted significant improvement in their tinnitus. Still others, however, have reported no such benefit.

A deficiency of vitamin B₁₂ can result in pernicious anemia, characterized by megaloblastic anemia, lack of intrinsic factor, inability to absorb vitamin B₁₂, and increased risk for esophageal webs and cancer. Because vitamin B₁₂ can be stored easily in the body and is only required in minute amounts, symptoms of severe deficiency usually take 3 to 5 years to appear. When symptoms do arise, usually in mid-life, it is likely that deficiency was caused by digestive disorders or malabsorption rather than poor diet. It is well known, however, that the elderly have a reduced dietary intake, which may predispose them to nutritional deficiencies. Furthermore, strict vegetarians (vegans) who do not consume any foods of animal origin need to supplement their diets with this nutrient because B₁₂ comes almost exclusively from animal sources.

Vitamin B₁₂ is available in supplemental form. Because of relatively poor gastric absorption, B₁₂ can be taken as a sublingual tablet or by injection. Supplements range in strength from 50 µg to 2 mg. Megadose vitamin B₁₂ toxicity is unknown, and any excess is excreted from the body [14]. One can measure serum B₁₂ or serum methylmalonic acid for levels of this vitamin. The normal range of B₁₂ in the healthy population is 150 to 900 pg/mL.

Experimental studies and clinical observations have related tinnitus to demyelination of nerve fibers and to a distorted resting state of spontaneous neural activity. Shemesh et al [14] showed a high prevalence (47%) of vitamin B₁₂ deficiency in patients with chronic tinnitus when a criterion of deficiency is set at 250 pg/mL and lower. Serum cobalamin deficiency was more widespread and severe in the tinnitus group associated with noise exposure. This suggested a relationship between vitamin B₁₂ deficiency and dysfunction of the auditory pathway. Deficiency also results in peripheral and central neurologic pathology. Decreased methionine production caused by cobalamin deficiency can lead to a sensory demyelinating neuropathy.

Abnormalities of the nervous system in the absence of hematologic disorders and normal results of the Schilling test have been reported in 28% of 141 consecutive patients with abnormally low serum cobalamin. The Schilling test assesses the absorption of free cobalamin and also the absorption of free cobalamin with intrinsic factor. In many instances, the actual cause of the deficiency is difficult to identify. It might be a result of inadequate dietary intake, a minor alimentary dysfunction, or a nutrition-metabolic disturbance. Supplemental cobalamin was found to show some relief in several patients with severe tinnitus [15].

Vitamin B₆ (pyridoxine)

Vitamin B₆ is a coenzyme involved in the metabolism of carbohydrates, fats, and proteins and the manufacturing of hormones, red blood cells, neurotransmitters, enzymes, and prostaglandins. It is also required for the production of serotonin, a neurotransmitter that controls mood, appetite, sleep patterns, and sensitivity to pain. A deficiency of vitamin B₆ can quickly lead to insomnia and profound malfunctioning of the central nervous system. Common symptoms of deficiency can include depression, vomiting, anemia, renal stones, dermatitis, lethargy, and increased susceptibility to diseases caused by a weakened immune system [8]. Among its many benefits include helping to maintain healthy immune system functions, protecting the heart from cholesterol deposits, and preventing renal stone formation. It is also beneficial in the treatment of carpal tunnel syndrome, premenstrual syndrome, night leg cramps, allergies, asthma, arthritis, and dizziness [8].

Supplemental B₆ is commonly used as a treatment for nausea, morning sickness, depression, and tinnitus. Natural foods that are highest in vitamin B₆ include brewers yeast, carrots, chicken, eggs, fish, avocados, bananas, brown rice, and whole grains. The RDI for vitamin B₆ is 2 mg/d. Most B-complex formulas contain between 10 and 100 mg of vitamin B₆. Vitamin B₆ is one of the few vitamins that can be toxic. Doses up to 500 mg/d are uncommon but safe. Doses above 2 g/d however, can lead to irreversible neurologic damage. Doses exceeding this level should not be used unless the patient is under the treatment of a physician. Vitamin B₆ supplements should not be taken by Parkinson's disease patients treated with L-dopa, because vitamin B₆ can diminish the effects of L-dopa in the brain.

Most of the vitamin B-complex supplements seem to work on tinnitus in some patients by providing a stabilizing effect on the nerves centrally and peripherally. Only anecdotal evidence exists regarding this treatment method.

Folic acid

Folic acid is a water-soluble nutrient belonging to the B-complex family. The name is derived from the Latin word "folium," because this essential nutrient was first extracted from green leafy vegetables, or foliage. Sometimes referred to as *vitamin M*, folic acid was originally extracted from spinach in 1941 and was found to be an effective treatment for macrocytic anemia [7].

Folic acid is a vital coenzyme required for RNA and DNA synthesis. Adequate levels are essential for energy production and protein metabolism, for the formulation of red blood cells, and for the proper functioning of the intestinal tract. Furthermore, studies have demonstrated that folic acid reduces homocysteine levels and reduces the risk of heart disease [8].

Additional studies revealed that maternal folic acid intake leads to a significant reduction in the incidence of fetal neural tube defects, such as spina bifida. This effect was noted with a daily folic acid intake of at least 400 µg, the current RDI. Folic acid may also prove to be effective in the prevention and treatment of uterine cancer [16].

Folic acid deficiency affects all cellular functions, but most importantly it reduces the body's ability to repair damaged tissues and grow new cells. Tissues with the highest rate of cell replacement, such as red blood cells, are affected first, leading to anemia. Deficiency leads to sore tongue; cracking at the corners of the mouth; gastrointestinal distress; diarrhea; and poor nutrient absorption, leading to stunted growth, weakness, and apathy [8]. Folic acid deficiency is common and can develop within a few weeks to months of lowered dietary intake. The greatest need for increased folic acid intake is in those who are under mental and physical stress, such as alcoholics, and people taking oral contraceptives, aspirin, or anticonvulsants. Foods highest in folic acid include barley, beans, beef, bran, brewers yeast, brown rice, cheese, chicken, green leafy vegetable, milk, salmon, tuna, wheat germ, and whole grains.

Although not generally regarded as toxic, large doses of folic acid can cause allergic skin reactions and should be avoided by people being treated for hormone-related cancers. High doses of folic acid can also cause problems in those taking phenytoin for a convulsive disorder. Folic acid seems also to have a stabilization effect on the nervous system. This might explain the anecdotal evidence regarding the supplementation of folic acid in certain patients to alleviate their tinnitus. The dosages used ranged from 400 to 800 µg/d and usually required 2 to 3 months of trial to achieve results [9].

Zinc

Zinc is a component of over 100 enzymes. Among these are DNA polymerase, RNA polymerase, and tRNA synthetase. Mild deficiency causes growth retardation in children. More severe deficiency is associated with growth arrest, hypogonadism, infertility, poor wound healing, diarrhea, dermatitis, alopecia, behavioral changes, taste and smell disorders, and tinnitus. Zinc seems to function in certain areas to influence neurotransmission and to inhibit binding of peptides and other ligands to their neuroreceptors.

The RDI of zinc in adults is 15 mg. Most of the zinc content in humans is bound to proteins in the tissues. In plasma, zinc is primarily bound to albumin; less than 2% of zinc is found free. The zinc level in serum is not the best parameter, but is the most reliable one for assessing zinc balance in the body. Nearly 99% of total-body zinc is inside the cells. The remainder is in plasma and extracellular fluids [17].

Studies on rodents have shown a high content of zinc in the inner ear. Other studies have found that the human cochlea has the body's greatest

concentration of zinc. These findings have given rise to speculation of the role of zinc in inner ear function. A correlation between hypozincemia and tinnitus has been reported [18]. In an uncontrolled trial by Gersdorff et al [19], zinc was found to reduce tinnitus. Zinc given in doses ranging from 10 to 25 mg has delivered good results in some patients shown to be hypozincemic based on blood tests. In a double-blind, randomized study, Paaske et al [17] showed little correlation between hypozincemia and tinnitus, and no significant improvement in subjective tinnitus using zinc supplements.

Ochi et al [18] demonstrated a significant decrease in zinc levels in patients suffering from tinnitus, and that supplementation with doses of 34 to 68 mg of zinc over 2 weeks significantly decreased tinnitus. Excellent results have been found with the combination of niacin and 25 mg zinc gluconate twice a day. If tinnitus is of recent onset, complete resolution is possible. With longer duration, the tinnitus can be diminished with these nutrients in some people.

Supplementation of 90 to 150 mg/d has been shown to be beneficial in some cases. Zinc therapy when prescribed is often accompanied by frequent blood tests to monitor copper levels. Copper and zinc compete for intestinal absorption, so chronic ingestion of zinc may result in copper deficiency. Acute zinc toxicity can usually be induced by ingestion of greater than 200 mg of zinc in a single day and is manifested by epigastric pain, nausea, vomiting, and diarrhea.

Calcium

By enhancing neural transmission, calcium supplementation has been shown to improve tinnitus symptoms in certain patients. Calcium is one of the most abundant minerals in the human body and accounts for between 2 and 3 lb of total body mass. Adequate dietary sources are necessary for building and maintaining strong bones and teeth and regulating muscle growth. In conjunction with magnesium, calcium also plays a pivotal role in the regulation of electrical impulses in the central nervous system and in the activation of various hormones and enzymes required for proper digestion and metabolism. This vital mineral is also necessary to support bodily functions, such as blood clotting and maintaining blood pressure. There is also strong evidence that calcium plays a role in colon cancer, and those with low intake of calcium and vitamin D are more prone to this disease.

Half of America's adults are not getting enough calcium according to a panel of experts assembled by the National Institutes of Health. The federal committee estimates that calcium deficiencies, resulting in brittle bones and fractures, are costing the US health care system \$10 billion annually. The report states that the recommended daily allowance for calcium is too low, leading to weak bones in children, adults, and especially elderly women [8].

Calcium absorption occurs primarily in the small intestines, and requires adequate amounts of vitamin D. The current RDI of calcium is 800 mg for adults, 1200 mg for premenopausal women, and 1500 mg for postmenopausal women unless they are taking estrogen. Those with kidney disorders should not take calcium supplements unless directed to do so by their health care professionals. Key dietary sources of calcium include dairy foods, green leafy vegetables, and seafood. Absorption of dietary calcium can be drastically reduced by consuming large amounts of such foods as cocoa; spinach; kale; rhubarb; almonds; and whole wheat products, which are high in oxalic acid, and are known to interfere with calcium absorption. Taking antibiotics, such as tetracycline, or aluminum-containing antacids can also result in lower absorption of calcium. Alcohol, sugar, and coffee can also affect the body's levels of this mineral.

Some patients have experienced improvement in their tinnitus after starting a regimen of vitamin and nutrient supplementation, which included calcium [9]. Dosages used ranged from 1000 to 1500 mg/d for several months.

Magnesium

Magnesium is the fourth most abundant cation in the body after sodium, potassium, and calcium, and the second most prevalent intracellular cation. The normal body content is around 1000 mmol, 50% to 60% of which is in bone. Extracellular magnesium accounts for only 1% of total body magnesium. The normal serum concentration ranges between 0.75 and 0.95 mmol/L [20].

Magnesium is essential for the function of important enzymes, including those related to the transfer of phosphate groups and every step related to the replication and transcription of DNA and the translation of mRNA. This cation is also required for cellular energy metabolism and has an important role in membrane stabilization, nerve conduction, and ion transport. Deficiency can result in a variety of metabolic abnormalities and clinical consequences, including tinnitus [1].

Magnesium has been shown to prevent hearing loss in a study by Attias et al [1]. Three hundred healthy, young male military recruits undergoing 2 months of basic training were studied. The trainees were repeatedly exposed to high levels of impulse noise. Each recruit received daily either 167 mg of magnesium (as magnesium aspartate) or a placebo (sodium aspartate). Permanent hearing loss was significantly more frequent and more severe in the placebo group. It can be inferred that magnesium may have a positive role on tinnitus.

Magnesium is a potent glutamate antagonist. There is evidence in the literature that antagonism of glutamate receptors has an effect on auditory sensitivity and on tinnitus [8]. Furthermore, a highly motivated patient elected to have magnesium sulfate delivered to the inner ear for her severe

unilateral cochlear tinnitus. While the MgSO_4 was being delivered, her tinnitus ceased. Unfortunately, it recurred shortly after cessation of the perfusion [9].

Animal studies have shown that noise exposure causes magnesium to be excreted from the body [20]. Supplementation with magnesium might reduce the ototoxicity from this noise and reduce the likelihood of new-onset tinnitus. Few studies have documented that magnesium supplementation improves tinnitus, but many patients have had relief with this method.

Manganese

Manganese is a mineral that is required in small amounts to manufacture enzymes necessary for the metabolism of proteins and fats. It also supports the immune system; regulates blood sugar levels; and is involved in the production of cellular energy, reproduction, and bone growth. Manganese works with vitamin K to support blood clotting and aids in digestion. As an antioxidant, manganese is a vital component of superoxide dismutase, an enzyme that is the body's main front-line defense against damaging free radicals [21]. Although there is no RDI for manganese, the average intake of manganese is between 2 and 9 mg/d. Foods high in manganese include avocados, blueberries, nuts and seeds, seaweed, egg yolks, whole grains, legumes, dried peas, and green leafy vegetables.

Along with the B-complex vitamins, manganese helps control the effects of stress while contributing to one's sense of well being, and it is possible that this may have a stabilizing effect on patients suffering from tinnitus. A deficiency in intake can retard growth; cause seizures; lead to poor bone formation; impair fertility; cause birth defects; and lead to nervous symptoms, such as tinnitus. Investigators are also looking at new links between manganese deficiency and skin cancers. Anecdotal evidence has shown that manganese supplementation may reduce the symptom of tinnitus [9].

Selenium

Selenium is a component of several enzymes, most notably glutathione peroxidase and superoxide dismutase. These enzymes prevent oxidative and free radical damage of various cell structures. Evidence suggests that the antioxidant protection conveyed by selenium operates in conjunction with vitamin E, because deficiency of one seems to enhance damage induced by a deficiency of the other. Selenium also participates in the conversion of thyroid hormone to its active form.

The RDI is 50 to 70 $\mu\text{g/d}$ [7]. Deficiency is rare in North America. Such individuals have myalgias, cardiomyopathies, and nervous system abnormalities. Keshan disease, a fatal heart disease found in children living in

certain sections of China, occurs where selenium intake is limited. Toxicity is associated with nausea, diarrhea, alterations in mental status, and peripheral neuropathy, observed in adults who inadvertently consumed between 1500 and 2700 mg. One may check red blood cell glutathione peroxidase activity, or plasma selenium concentrations for deficiency, although neither is entirely accurate [22]. Supplementation may take up to 6 months to show improvement in symptoms, such as tinnitus.

Hyperbaric oxygen therapy

Oxygen deprivation or reduced cochlear blood flow has been suggested as a potential cause of hearing loss and tinnitus in response to intense noise exposure or secondary to sudden sensorineural hearing loss. Hyperbaric oxygen therapy may be considered in these situations. It may be more effective for recent-onset rather than long-term cases. Because tinnitus and hearing loss are not approved indications for the use of hyperbaric oxygen therapy, insurance does not normally cover the treatments. Hyperbaric oxygen therapy is commonly used in European countries for the management of sudden hearing loss and noise-induced hearing loss and the results have been positive [23].

The theory behind hyperbaric oxygen therapy treatment is based on the assumption that tinnitus is caused by reduced oxygenation to the inner ear. Studies at Munich Technical University have shown that pure oxygen treatment under high air pressure can increase oxygen saturation in the inner ear up to 500%. In Russia this method reportedly has been used with success for many years. In Moscow alone, there are about 40 pressure chambers in use for this currently [24].

Vinpocetine and vincamine

Vinpocetine is a derivative of vincamine, which is an extract of the periwinkle. Although they have many similar effects, vinpocetine has more benefits and fewer adverse effects than vincamine. It is a vasodilator and increases blood flow to the brain and improves the brain's use of oxygen [25].

These drugs have not yet been approved for treatment in the United States; however, they are available in Europe and South America in over-the-counter preparations. Although not available in North America as a pharmaceutical, they are available in low doses in over-the-counter supplements. Only anecdotal evidence exists that these medications can suppress tinnitus [9].

Vinpocetine is a derivative of vincamine and is three to four times more potent at improving cerebral circulation and is overall twice as potent as vincamine in humans. Vinpocetine has wide ranging effects and can be used

to treat stroke and improve memory, menopausal symptoms, macular degeneration, impaired hearing, and tinnitus. The usual oral starting dose is 40 mg three times daily, to be followed by a maintenance dose of one 20 mg tablet three times daily for a longer period of time. Vinpocetine has not been reported to interact with other drugs.

In humans, the effect of vinpocetine on cerebral blood flow is uncertain, with some investigators reporting no change and others reporting an increase. It has been reported that vinpocetine can be used safely to treat patients with “chronic cerebral dysfunction of vascular origin.” Vinpocetine is also a powerful memory enhancer. It facilitates cerebral metabolism by improving cerebral microcirculation, enhancing brain cell ATP production, and increasing use of glucose and oxygen [25]. Vincamine has also been used to treat a remarkable variety of conditions related to insufficient blood flow to the brain, including vertigo and Meniere’s syndrome, difficulty in sleeping, mood changes, depression, hearing problems, high blood pressure, and lack of blood flow to the eyes [26]. Vincamine has also been used for improving memory defects and inability to concentrate. Vincamine has extremely low toxicity and is inexpensive.

Hydergine

Hydergine is reported to increase mental abilities, prevent damage to brain cells from hypoxia, and may even be able to reverse existing damage to brain cells. Hydergine is an extract of ergot, a fungus that grows on rye [27]. Midwives in Europe traditionally used ergot with birthing mothers to lower their blood pressure. Scientists have analyzed ergot alkaloids since the late 1940s in search of blood-pressure medications. Studies in the elderly population uncovered cognition-enhancing effects of Hydergine and it is now a popular treatment for all forms of senility in the United States, and is used to treat a plethora of problems elsewhere in the world.

Hydergine probably has several modes of action for its cognitive-enhancement properties. Its wide variety of reported effects includes the following: increases blood supply and oxygen to the brain, enhances brain cell metabolism, protects the brain from free-radical damage during decreased or increased oxygen supply, and reduces symptoms of dizziness and tinnitus [28].

Hydergine may cause mild nausea, gastric disturbance, and headache. There are no serious side effects reported with Hydergine use. It is nontoxic even at very large doses. It is contraindicated for individuals with acute or chronic psychosis, however, or those with a known sensitivity to the medication. Overdosage may, paradoxically, cause an amnesic effect.

Hydergine is available in the United States with a prescription. Hydergine has not undergone rigorous scientific tests to prove its effectiveness for tinnitus reduction. In Europe, however, many patients have been using Hydergine with good success in relieving their symptoms.

Herbal remedies

Patients who suffer from the condition of tinnitus have the opportunity to explore the horizon of CIM in pursuit of a treatment regimen that may relieve many of their agonizing symptoms. As is the case in the treatment of other chronic diseases, conventional pharmacotherapy represents only one avenue on which the physician may venture. In an attempt to relieve the symptoms that plague the common tinnitus patient, the patient may want to explore nonconventional treatment options.

For more than 2000 years, herbal regimens have been used in the treatment of medical conditions [28]. Combinations of Chinese herbs, exotic fruits, plant roots, and seed oils have proved to be effective in the treatment of many medical disorders where conventional medical therapy has failed. What many of these herbal treatment regimens lack is solid medical evidence in the form of double-blind research experiments, which legitimize the use of these nonconventional treatments. To the suffering patient whose treatment regimens have been met with failure, however, perhaps anecdotal accounts of effective treatments are proof enough to justify an alternative approach.

Ginkgo biloba

Ginkgo biloba, or maidenhair, is the oldest living tree on earth. *G. biloba* leaves have been used therapeutically by the Chinese for centuries for the treatment of asthma and bronchitis. *G. biloba* was believed at one time to have magical powers. Today, ginkgo is believed by many to have a legitimate medicinal role. The important components of ginkgo are flavonoids and terpenoids. These have been shown to inhibit the action of platelet-activating factor. The putative active ingredient has been isolated as EGB761 and there have been many studies related to its effectiveness in a variety of medical disorders [29]. It has been shown to increase circulation throughout the body. Numerous studies have shown the efficacy of ginkgo on intermittent claudication, cerebral insufficiency, and tinnitus [30].

Typical dosages range from 120 to 480 mg/d, divided equally at mealtime. In western countries a standardized 50:1 concentrate of 24% ginkgo flavonoids is used, either in liquid or capsule form. Most studies showed that between 30% and 70% of subjects had improved cognitive abilities over a 6- to 12-week period [29]. No serious side effects were observed, and any minor side effects were not statistically significant compared with subjects treated only with placebo.

In terms of tinnitus, a study by Hobbs [29] in 1986 provided statistical significance for the effectiveness of treatment with ginkgo extract for tinnitus; the ringing completely disappeared in 35% of the patients tested, with a distinct improvement in as little as 70 days. Similarly, when 350

patients with hearing defects caused by advanced age were treated with ginkgo extract, the success rate was 82%. Furthermore, a follow-up study of 137 of the original group of elderly patients 5 years later revealed that 67% still had better hearing [30].

Opinions differ as to the efficacy of this herbal remedy. Whereas certain sufferers of tinnitus swear by *G. biloba*, others claim that it has no effect on their symptoms. The results of the first large-scale double-blind randomized prospective study (1121 volunteers at Birmingham University in the United Kingdom) on the efficacy of ginkgo in tinnitus treatment was published in 2001. The patients in this study received either 150 mg of ginkgo or placebo in a randomized fashion for 12 weeks. The results did not show a significant effect in treating tinnitus; however, the dose used was approximately 65% less than what has been shown to be of benefit [31].

Published studies have shown that 120 to 240 mg twice per day of pharmaceutical-grade ginkgo extract can alleviate tinnitus [32]. A controlled study showed that ginkgo extract caused a statistically significant decrease in behavioral manifestation in the animal model of tinnitus. Another human study showed that in patients suffering from cerebrovascular insufficiency, ginkgo extract produced a significant improvement in symptoms of vertigo, tinnitus, headache, and forgetfulness [26,29].

One of the appealing aspects of *G. biloba* with regard to the treatment of tinnitus has been the fact that it is relatively inexpensive, and has negligible side effects, such as increase risk for epistaxis. There has been one report of a woman who used ginkgo for approximately 2 years who developed a subdural hemorrhage [9]. This substance, however, has been used for more than 2000 years without severe side effects. As with any medication, the physician should take a careful history before recommending ginkgo because it may potentiate hemorrhage in people taking warfarin or heparin. The German Commission E, which is considered an excellent reference for the medicinal use of therapeutic herbs, rates ginkgo as positive and recommends 240 mg twice per day for tinnitus and vertigo [26]. The response to ginkgo can occur within weeks, but is most noticeable within 3 to 4 months.

Combined application of soft-laser irradiation of the cochlea and intravenous supply of ginkgo extract for 4 weeks was found to be beneficial in 20% to 50% of patients in one study [33]. The mechanism of the soft laser is unknown, but it is known to cause an athermic stimulation of biochemical processes induced by light. Increased ATP production occurs in yeast fungus cultures irradiated with the soft laser, yet it is unclear if it is this same mechanism in human inner ear cells. Soft-laser–ginkgo therapy promised to be very effective in chronic tinnitus. Ginkgo provides a better oxygen supply and the laser acts directly on the flavoproteins to activate repair mechanisms. Plath and Olivier [33] showed that in single cases, tinnitus reduction can be attained and they deduced that combined soft laser and ginkgo application can be helpful in some patients suffering from severe tinnitus.

Wedel et al [34], however, showed no significant improvement with these treatments compared with placebo.

The variable response to herbs including ginkgo raises the concern of whether all preparations are the same. In the senior author's experience, it is clear that some of the less expensive brands were ineffective and had a higher rate of gastrointestinal upset. When these patients were then changed to a more respected or well-known brand, these side effects were ameliorated and the patients' response typically was better. Over the past several years, we have been recommending Arches Tinnitus Relief Formula (www.tinnitusformula.com), because their formulation is highly standardized and seems to be effective for some patients. Ginkgo is not effective in every patient with tinnitus, but the risk to benefit ratio suggests that a trial with ginkgo is reasonable.

Black cohosh (Cimicifuga racemosa)

The popular herb black cohosh comes from the root of the North American forest plant *Cimicifuga racemosa*. It derives its name from a description of the rhizome, which is black and rough. Also known as black snakeroot, bugbane, bugwort, and squawroot, black cohosh has an extensive history of safe use by Native Americans who revered it as a remedy for a host of common ailments [26]. Native Americans used black cohosh as an effective treatment for fatigue, neuralgia, rheumatism, sore throat, asthma, bronchial spasms, bronchitis, and whooping cough. Mixed with chamomile, ginger, and raspberry leaf, black cohosh has been used for centuries by women to stimulate menstrual flow, ease the strains of childbirth, and confer relief from the symptoms of menopause.

Contemporary herbalists also hold black cohosh in high regard as an antispasmodic for relief from cramps, muscle pains, and menstrual pains. With its mildly sedative and relaxing effect, black cohosh is also used to treat anxiety, nervousness, and chronic tinnitus. Some patients have reported improvement in their tinnitus while using this herbal preparation.

The active ingredients in black cohosh seem to be chemical derivatives mimicking some of the effects of estrogen. It was also found to contain the glycoside acetin, a steroidal derivative that is effective in lowering blood pressure in animals [4]. Black cohosh also contains compounds that support its use as a sedative and as an anti-inflammatory agent.

There are few known health concerns regarding black cohosh, but consuming large amounts is known to cause nausea, dizziness, and vomiting. Expectant mothers should only use black cohosh under the supervision of a health professional, because it has a reputation of stimulating the uterus to contract, and large doses could lead to premature birth. Black cohosh has traditionally been used to calm the nervous system by nourishing blood vessels [3] and it is theorized that it may improve cerebral

blood flow, providing relief from tinnitus in some patients. Dosages range from 20 to 40 mg/d in liquid form for this ailment.

Mullein (Verbascum densiflorum)

Mullein is ubiquitous, and its velvety leaves, rod-like stem, and brilliant yellow flowers are its striking characteristics. Mullein has a long history of use in herbal medicine. Its botanical family name (Scrophulariaceae) is derived from *scrofula*, an old term for chronically swollen lymph glands, later identified as a form of tuberculosis. Initially, this herb gained a favorable reputation as a respiratory remedy. Physicians from India to England touted it as a treatment for coughs and chest congestion, alleviating irritation, earaches, and tinnitus [35].

In a 1986 survey of folk medicine in Indiana, researchers discovered that this herb remains very popular for respiratory complaints [35]. There has been little research on mullein itself, and even less research into its treatment of tinnitus. Some herbalists have shown benefit in patients suffering from severe tinnitus, however, claiming it to be very valuable. Mullein seems to have a slight diuretic effect and may alleviate inflammation. To brew a medicinal tea, use one to two teaspoons of dried leaves per cup of boiling water. Boil for 10 minutes and strain leaves. One teaspoon contains approximately 0.5 g of the drug. The dosage reported to provide relief from tinnitus seems to be 3 to 4 g/d. There have been no reports of mullein causing adverse effects, except for mild irritation of the skin when in contact with the living plant [4].

Cornus

Cornus, which is also known as Asiatic cornelian cherry fruit and Asiatic dogwood, is grown in several parts of China. The fruit is harvested in October and November when it becomes purplish red, and is fat, thick, soft, and seedless. Available at Chinese pharmacies, Asian food markets, and some Western health food stores, cornus is taken internally for excessive urination, incontinence, impotence, lightheadedness, excessive sweating, and excessive menstrual bleeding. Formerly, it was in use as a replacement for quinine [3]. Preparation of the combination formula alluded to, which is used in the treatment of tinnitus, requires the consultation of an herbalist. Chinese herbalists advise against the usage of cornus in combination with several other herbs, including platycodon, siler, and stephania.

Cornus (*Cornus officinalis*) alone does not seem to relieve the symptoms of tinnitus, but when used in combination with Chinese foxglove root and Chinese yam proves to be effective in the treatment of tinnitus, low-back pain, and urinary frequency [4].

Other therapies

Wobenzym

Wobenzym is a group of proteolytic enzymes including pancreatin, trypsin, chymotrypsin, bromelain, papain, and rutosid. It was initially developed by Ransberger in 1959 with MUCOS Pharma to fight cancer. Ransberger brought the formula to Germany and since then has pioneered the medical use of the systemic enzymes. This remedy has shown effectiveness for arthritis, throbbing pains, and tinnitus. It seems to be an alternative to aspirin and has shown some benefit to recovering from a myocardial infarction [36].

Studies in Europe have been conducted on Wobenzym, backing the findings of Ransberger. Studies show Wobenzym to be safe with none of the adverse side effects of aspirin, ibuprofen, and other nonsteroidal anti-inflammatory drugs [37]. It has also been shown to improve red blood cell viscosity, improve circulation to damaged areas, and have anti-inflammatory properties [37]. Whether or not Wobenzym can positively influence the symptom of tinnitus has not been adequately studied, but some patients have noted relief.

Laser therapy

In the cochlea, all of the auditory processes require energy in the form of ATP. ATP is produced by the mitochondria inside each cell. If the cochlea is acutely or chronically overstrained, its sensory cells and their various cellular organelles also are affected, and they inevitably lose part of their functional capacity. The cells may suffer from a lack of ATP. This continuous lack of ATP within the inner ear cells of the cochlea leads either to a gradual or sudden impairment of the entire hearing organ.

Using low-level laser therapy, Wilden in Germany has been able to produce a positive biologic reaction regardless of the dysfunction involved in the inner ear. The electromagnetic energy released by the oxidation of nutrients is used as a source of primary energy for the production of the cellular fuel ATP.

The mitochondria can, in addition to the absorption of the released metabolic energy, use both the photons of the natural solar radiation (apparent biostimulative effect of sunlight on human cells) and the photons of low-level laser light as a source of primary energy. Wilden uses two separate beams on the mastoid bone and one beam down the ear canal simultaneously. This delivers a calculated 4 J/cm^2 to the cochlea [38]. The additional ATP triggered by the light may have some healing value for the damaged inner ear hair cells. This therapy may be more beneficial in patients in the early stages of tinnitus because it may have more benefit in damaged cells than dead ones.

Betahistine hydrochloride

Betahistine hydrochloride, also known as *Serc*, is not approved for use in the United States. This drug has been used in Canada and Europe for patients

with severe vertigo from Meniere's disease and in some patients suffering from tinnitus. Betahistine was found to have a histamine-like action in animals.

The usual starting dose is 4 mg three times per day and may increase up to 48 mg/d. Side effects include headaches (usually in the first 1 to 3 days of treatment) and it is relatively contraindicated in patients with ulcer disease. Some studies in the past have shown efficacy in treating vertigo and tinnitus. An abstract by Martin [39] compares betahistine, pentoxifylline, and xantinol-nicotinate in the treatment of tinnitus. Using 172 patients, the results showed that those receiving betahistine produced significantly better therapeutic results in eliminating their tinnitus.

Vibrational therapy

Tinnitus may arise from damage to the microscopic endings of the hearing nerve in the inner ear. The health of these nerve endings is important for acute hearing, and injury to them brings on hearing loss and tinnitus. Advancing age is generally accompanied by a certain amount of hearing nerve impairment and often tinnitus.

A device has been developed in Europe by DiMino. He suffered from tinnitus and pioneered the Aurex-3 (ADM Tronics Unlimited, Inc., Northwale, NJ), which stimulates the damaged nerve endings in a broadband frequency surrounding the frequency of the tinnitus. Eventually the brain is retrained to not reproduce the original tinnitus sound at the same intensity.

Mechanical vibrations are generated in the applicator and transmitted into the cochlea by placing the probe in front of the mastoid bone just behind the ear. A primary vibration is applied and its frequency tuned until it best matches or masks the tinnitus sound. Because different parts of the cochlea operate at different frequencies it is important to ensure that the treatment is targeting the damaged area within the ear. The amplitude of vibration is then raised to a tolerable level for the patient, increasing the energy applied to the damaged area.

The manufacturers of Aurex-3 recommend initial treatments of 3 to 5 minutes' duration, three to four times a day. Immediate relief is rarely experienced but after regular use of 4 to 6 weeks' period, relief should be sufficient to reduce the frequency of ongoing treatments. For those people who experience unilateral tinnitus, treatment in just one ear is appropriate. For those who experience bilateral tinnitus or tinnitus inside their head, however, it is recommended that both ears be treated.

The Aurex-3 represents a new alternative for the potential relief from tinnitus. Experience from use of this device has shown good results and on the basis of subjective evidence the Aurex-3 is being promoted as a new development in the treatment of tinnitus.

Clinical trials are now underway to more substantiate evidence of these results and to determine precisely the effectiveness of effective Aurex-3. Trials are being conducted in the United States and in Europe [40].

Tinnitus retraining therapy

Jastreboff and Jastreboff [41] have developed a therapy technique called tinnitus retraining therapy, which has provided significant improvement for at least 80% of tinnitus sufferers. Tinnitus retraining therapy is based on strong neurophysiologic evidence that any person can habituate to acoustic, or acoustic-like, sensations in their environment.

Tinnitus retraining therapy has two key elements: directive counseling and sound therapy. The counseling session is critical to the success of the program, and patients may actually achieve relief through counseling alone. The counseling process involves an in-depth discussion of the hearing physiology, which helps the patient understand why tinnitus occurs. Hearing only starts at the ear; from there, sound signals travel to the lowest levels of the brain (brainstem) and pass upward to arrive eventually at the highest level of the brain, the auditory cortex. Random signals in these areas may be responsible for the perception of tinnitus. A strong negative emotional reaction to the tinnitus causes it to be a problem. An expanded discussion about the auditory process enlightens patients and helps relieve their fears.

In addition to counseling, most patients are fitted with ear-level white noise devices. These look like small hearing aids and are comfortably worn during the day. The sound is set to a very low level, which never interferes with normal hearing, and after several weeks most patients do not hear the sound unless they really try to hear it. These devices help the brain to ignore the random signals of tinnitus, achieving auditory habituation.

The initial evaluation and counseling process is quite extensive, usually lasting 4.5 to 5 hours. Regular follow-up visits or telephone communication for out-of-town patients are absolutely necessary. Within 6 to 24 months many patients have eliminated or are no longer bothered by their tinnitus.

Summary

Tinnitus is a significant medical problem affecting approximately 50 million Americans, 12 million of them severely. Once a thorough evaluation has been performed by a qualified otolaryngologist, and no life-threatening pathology has been identified, the opportunity for treatment exists. Treatment options are extensive and range from approved protocols to anecdotal remedies. Although tinnitus may not miraculously disappear, many therapeutic options exist that may help to make the tinnitus more manageable.

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