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Key Inforbits

- Consequences of Insufficient Sleep
- Role of Pharmacists and Techs
- Future of Sleep Aids
- OTC Sleep Aids Background
- Latest News on Sleep Aids

Over-the-Counter (OTC) Sleep Aids

Image from: https://stock.adobe.com/search?k=peaceful+sleep+night

Consequences of Insufficient Sleep

Approximately 32.8% of adults don't get enough sleep.[1] Lack of sleep can cause daytime sleepiness, fatigue, irritability, and even hallucinations.[2] Poor sleep has also been linked to high blood pressure, type 2 diabetes, increased risk of heart attack or coronary heart disease, and even weight gain or obesity.[1] These adverse effects of insufficient sleep also have economic consequences. Sleep deprivation has been shown to elevate mortality risk and contribute to significant declines in workplace productivity. According to one study, this costs the U.S. up to $411 billion a year.[3]

OTC products and supplements for sleep:

OTC Products:

Diphenhydramine

Diphenhydramine is a first-generation antihistamine with significant sedative properties that is used as a sleep aid for **transient** and **short-term** sleep difficulties.[4] It was approved in 1946 as the first prescription antihistamine, then was later approved as an OTC product in the 1980s.[5] It works by competitively blocking histamine-1 receptors.[4] Peak sedation typically occurs 1–3 hours after a dose is taken. For individuals 12 years old and older, the usual sleep-aid dose is 50 mg taken about 30 minutes before bedtime. It's important to be aware of clinically significant drug–drug interactions when using diphenhydramine. Common side effects include dry mouth and throat, constipation, blurred vision, urinary retention, and tinnitus. Diphenhydramine is also found in various combination products with acetaminophen, ibuprofen, or aspirin. Examples include Advil PM Pain Reliever & Nighttime Sleep Aid, Excedrin PM Headache, and Tylenol PM Extra Strength.

Doxylamine

Doxylamine is another first-generation antihistamine commonly used as an OTC sleep aid. It was approved for OTC sales in 1978.[6] There is limited evidence supporting doxylamine's efficacy as a sleep aid. The typical adult dose for sleep is 25 mg taken before bedtime. Like diphenhydramine, it produces sedation by competitively inhibiting histamine-1 receptors.[4] Side effects are similar to diphenhydramine and include dry mouth and throat, constipation, blurred vision, urinary retention, and tinnitus. It is found in the OTC product Unisom SleepTabs (doxylamine succinate).[6]

Dietary Supplements:

Melatonin

Melatonin is a naturally occurring hormone synthesized primarily in the pineal gland, with production triggered at night under normal light-dark conditions. Its nightly secretion is driven by the internal "clock" in the suprachiasmatic nucleus (SCN), which senses light input from the retina and synchronizes melatonin release to environmental light–dark cycles.[7]

Melatonin's best-known role is regulating the body's circadian rhythm and sleep wake cycle: it helps initiate sleep and signals nighttime to the brain by acting on melatonin receptors (MT1 and MT2), dampening wake-promoting signals. Beyond sleep, melatonin exhibits antioxidant, anti-inflammatory, and neuroprotective properties scavenging free radicals, reducing oxidative stress, modulating immune responses, and potentially protecting against neurodegenerative processes. It may also influence metabolic cycles, energy balance, and cardiovascular and reproductive physiology.[7]

As a supplement, exogenous melatonin is often used to improve sleep quality, shorten time to fall asleep, and treat certain circadian rhythm disturbances (jet lag, delayed sleep phase). It has been available as an OTC product since 1994 in the United States.[8] Melatonin is found in the OTC products such as Melatonin Time Release, SGard, VesPro Melatonin, Sleep3, and Bio-

Melatonin.[9] Its safety profile is generally favorable, with most studies showing good tolerability when used short-term. However, data on long-term use are limited. Concerns include potential effects on reproductive hormones, puberty timing in children, and possible interactions with anticoagulants, antiepileptics, and immunomodulating agents. Chronic nightly use may also alter natural melatonin secretion patterns, and emerging observational data including a recent analysis presented at the 2025 American Heart Association Scientific Sessions that reported a possible association between ≥1 year of melatonin use and increased heart failure risk underscore the need for large, long-term studies with prespecified cardiovascular end points. These studies are needed to clarify whether chronic melatonin exposure has neutral, protective, or harmful effects on outcomes such as heart failure, myocardial infarction, and stroke, particularly in older adults. Overall, while melatonin is considered safe for intermittent or short-duration use, the long-term risks and optimal maintenance dosing remain unclear.[7]

Valerian

Valerian is a natural product derived from plants in the *Valeriana* genus, which is native to Europe and Asia.[4] Valerian has been used medicinally since ancient Greek and Roman times.[11] It is used to help with insomnia and anxiety. Valerian contains valeric acid and other compounds that are believed to interact with GABA receptors in the brain, producing a sedative effect. Most clinical studies have used doses ranging from 400–900 mg taken 30–120 minutes before bedtime. Valerian can also be consumed as tea made from the plant's dried roots. Reported side effects include headache, excitability, and occasionally paradoxical insomnia. Withdrawal symptoms have been noted after discontinuation, and long-term use has been associated with hepatotoxicity. Valerian should not be combined with other central nervous system depressants due to the risk of adverse events. There is limited evidence supporting the effectiveness of valerian.

Chamomile

Chamomile is a natural supplement derived from the flower of the German Chamomile plant. It has been used medicinally since Roman times.[12] It contains bioactive compounds like flavonoids and terpenoids.[13] It is believed that its sedative effect is due to binding to a benzodiazepine and gamma-aminobutyric acid (GABA) receptors. It can be consumed as a supplement or tea and there is no specific dosing recommendation due to a lack of data. There is also limited data on side effects. Reported side effects include dizziness, nausea, disturbance in menstrual cycle, and allergic reactions. Of note, chamomile is contraindicated in patients with a hypersensitivity to ragweed pollens.[12] It may increase the anticoagulation effect of warfarin.

Ashwagandha

Ashwagandha is a natural supplement derived from the *W. somnifera,* a plant grown in India, the Middle East, and Africa. Historically it has been used as an adaptogen, diuretic, and sedative. A chemical constituent of the plant, withaferin A has multiple reactive sites that are thought to be potential therapeutic targets. The studied dose for sleep quality is 300 mg twice daily for 10 or 12 weeks. There is limited data on adverse reactions with ashwagandha, although there have been reports of ashwagandha-induced liver injury.[14]

OTC Medication Summary		
Product	**Dose**	**ADRs**
Over-the-Counter Medications		
Diphenhydramine	50 mg 30 minutes before bedtime	Dry mouth and throat, constipation, blurred vision, urinary retention, and tinnitus
Doxylamine	25 mg before bedtime	Dry mouth and throat, constipation, blurred vision, urinary retention, and tinnitus
Supplements		
Melatonin [15]	1-10 mg nightly up to 4 weeks	Headache, dizziness, nausea, stomach cramps, irritability, nightmares, and daytime somnolence
Valerian	400–900 mg taken 30–120 minutes before bedtime	Headache, excitability, and occasionally paradoxical insomnia
Chamomile	No specific recommendation	Dizziness, nausea, disturbance in menstrual cycle, and allergic reactions
Ashwagandha	300 mg twice daily for 10 or 12 weeks	Potential liver injury (limited data)

Latest News on Sleep Aids

Melatonin safety and cardiovascular concerns (2025):
A new observational analysis presented at the American Heart Association (AHA) Scientific Sessions 2025 reported a possible association between long-term melatonin use (one year or more) and an increased heart failure risk. This finding is preliminary, based on a meeting abstract, and has not yet undergone peer review. Because long-term safety data for melatonin remain limited most clinical studies have evaluated short-term use ranging roughly 2–12 weeks with relatively small sample sizes evidence on chronic nightly use and cardiovascular outcomes remains insufficient. This highlights the need for more robust long-duration trials assessing safety beyond short-term improvements in sleep.

Herbal agents (2024–2025):
Ashwagandha continues to be studied for sleep improvement. A 2021 meta-analysis showed modest improvement in sleep quality at doses of 600 mg per day or higher.[11] Clinical trials are now evaluating sustained-release ashwagandha and combination supplements. Data from national surveys referenced in the bulletin indicate that Americans increasingly rely on OTC sleep supplements over antihistamine-based products, with melatonin remaining the most commonly used agent, reflecting its continued rise in use.[16,17]

Usage trends:
OTC sleep aids are available in several forms, including antihistamine-based products and supplements such as melatonin, valerian, chamomile, and ashwagandha. Melatonin is widely recognized and frequently used as a first-line option among OTC supplement-based sleep aids, while antihistamines like diphenhydramine and doxylamine remain common choices for short-term use.

Future of Sleep Aids

There are several ongoing U.S. clinical trials evaluating the use of OTC sleep aids. One randomized controlled trial (not yet recruiting) is designed to assess the effects of sustained-release ashwagandha 150 mg compared with placebo in individuals experiencing disturbed sleep. The trial is expected to be completed by March 2026.[18] Another trial is examining three different combination sleep supplements versus placebo, two of which include ashwagandha as a key ingredient. This study is currently active and was estimated to be completed by October 2025.[19] A recent meta-analysis investigating ashwagandha's impact on sleep found that it produced a modest improvement in overall sleep quality, with the greatest benefits seen at doses of ≥ 600 mg per day.[16] However, the authors stressed that additional safety data are needed before ashwagandha can be recommended for long-term use for sleep-related concerns.

Nonpharmacologic/Sleep Hygiene

Sleep is vital for health and daily functioning. Before treatment options consider non-pharmacological approaches to improve sleep such as sleep hygiene. Sleep hygiene is "modifiable behaviors that can be beneficial or detrimental to sleep.[17] The Sleep Foundation offers several helpful tips for building healthy sleep hygiene habits that pharmacists can share with patients.[20]First, establish a consistent sleep schedule by choosing a fixed bedtime and wake-up time and make sleep a priority. Create a calming nightly routine by spending about 30 minutes winding down without computer/phone/TV screens and dimming the lights. Support your natural circadian rhythm with good daytime habits, such as getting exposure to natural light and engaging in regular physical activity. Limit nicotine and alcohol and avoid caffeine later in the day. It's also important to optimize your sleep environment. Use a comfortable mattress, pillows, and sheets, and aim to keep your bedroom temperature around 65 degrees Fahrenheit.

These strategies can improve sleep quality, but they may not resolve all sleep issues. Some individuals may need additional evaluation or treatment for persistent sleep problems.

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The last "dose" …

"No day is so bad it can't be fixed with a nap" –

Carrie Snow, 1953 - (American stand-up comedian, writer, author)

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