Drug Therapy for Anxiety and Insomnia:

The clinical manifestations of these disorders are similar and overlapping; that is, daytime anxiety may be manifested as nighttime difficulty in sleeping because the person cannot "turn off" worries, and difficulty in sleeping may be manifested as anxiety, fatigue, and decreased ability to function during usual waking hours.

Pathophysiology of anxiety disorders is imbalances among several neurotransmission systems. A simplistic view involves an **excess** of excitatory neurotransmitters (e.g., norepinephrine) or a **deficiency** of inhibitory neurotransmitters (e.g., gamma-aminobutyric acid [GABA]). GABA is the major inhibitory neurotransmitter in the brain and spinal cord. Gamma-aminobutyric acid A (GABAA) receptors are attached to chloride channels in nerve cell membranes.

Sleep is a recurrent period of decreased mental and physical activity during which a person is relatively unresponsive to sensory and environmental stimuli. Normal sleep allows rest, renewal of energy for performing activities of daily living, and alertness on awakening.

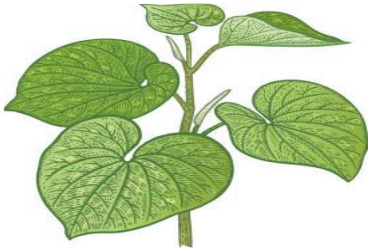
Insomnia, prolonged difficulty in going to sleep or staying asleep long enough to feel rested, is the most common sleep disorder. Insomnia is said to be chronic when it lasts longer than 1 month.

When a person retires for sleep, there is an initial period of drowsiness or sleep latency, which lasts about 30 minutes. After the person is asleep, cycles occur approximately every 90 minutes during the sleep period. During each cycle, the sleeper progresses from drowsiness (stage I) to deep sleep (stages III and IV).

These stages are characterized by depressed body functions, non-rapid eye movement (non-REM), and nondreaming, and they are thought to be physically restorative. Activities that occur during these stages include increased tissue repair, synthesis of skeletal muscle protein, and secretion of growth hormone. At the same time, there is decreased body temperature, metabolic rate, glucose consumption, and production of catabolic hormones. A period of 5 to 20 minutes of REM, dreaming, and increased physiologic activity follows stage IV.

Herbal Supplements Commonly Used to Reduce Anxiety and Insomnia:

1. Kava:



2. Melatonin:

This Endogenous hormone is produced by the pineal gland, an endocrine gland in the brain. In addition to its endogenous functions as a hormone and antioxidant, melatonin is also administered exogenously as a dietary supplement and medication. Melatonin is used medically primarily for sleep-related problems. It is used in the treatment of sleep disorders, including insomnia and various circadian rhythm sleep disorders. Exogenous preparations are produced synthetically and may contain other ingredients. Melatonin products are widely available.

Recommended doses on product labels usually range from 0.3 to 5mg

3. Valerian:

Drug Therapy:

The main drugs used to treat insomnia are the benzodiazepines and the nonbenzodiazepine hypnotics. Benzodiazepines are widely used for anxiety and insomnia and are also used for several other indications.

These drugs have a wide margin of safety between therapeutic and toxic doses, and they are rarely fatal, even in overdose, unless combined with other CNS depressant drugs, such as alcohol.

•Diazepam (Valium) is the prototype benzodiazepine.

•Alprazolam is administered orally to reduce anxiety and panic disorders.

•Chlordiazepoxide is most commonly administered for the control of withdrawal symptoms related to acute alcoholism.

Nonbenzodiazepine sedative–hypnotic agents:

- **Eszopiclone** is the first oral nonbenzodiazepine hypnotic to receive FDA approval for long-term use (≤12 months).
- **Ramelteon,** a melatonin agonist, is used for the long-term treatment of insomnia characterized by difficulty with sleep onset.

Drug Therapy for Seizure Disorders: Epilepsy:

Sudden, abnormal firing of neurons is characteristic of epilepsy. Signs and symptoms of seizure activity lead to the diagnosis. On the electroencephalogram (EEG), abnormal brain wave patterns are present. **Epilepsy** classifies seizures as partial or generalized.
Partial seizures begin in a specific area of the brain and often indicate a localized brain lesion such as birth injury, trauma, stroke, or tumor. **Generalized seizures** are bilateral and symmetric, with no visible point of origin in the brain.

Drugs Administered for Seizures (Antiepileptic Drugs):

1. **Phenobarbital** is the prototype AED of the **barbiturate class**. Since its development in 1912, it has been used as an antiepileptic or sedative.
2. **Benzodiazepines:** Drugs belonging to this class have a broad range of uses; they may act as sedatives, antiepileptics, or skeletal muscle relaxants and hypnotics.

The **benzodiazepines** potentiate the effects of **GABA** by increasing the attraction to the receptor sites:

- **Diazepam**
- **Clobazam**
- **Clonazepam**
- **Clorazepate**

3. Gamma-aminobutyric acid Structural analogs:

Gabapentin for the treatment of partial seizures. In May of 2002, the FDA approved it for the treatment of neuralgia pain.
Pregabalin is administered for partial-onset seizures, neuralgia, neuropathic pain, and neuropathy associated with diabetes.
Tiagabine is an adjunctive therapy for partial seizures
Vigabatrin received FDA approval for the treatment of infantile spasms.

4. Hydantoins:

The prototype antiepileptic of the hydantoin class is **Phenytoin**
The oldest and most widely used AED, it is often the initial drug of choice, especially in adults. In addition to using it to treat seizure disorders, prescribers sometimes order it for cardiac dysrhythmias.

5. **Iminostilbenes:** The AEDs classified as the iminostilbenes include:
    - The prototype **Carbamazepine** (Tegretol).
    - **Oxcarbazepine** has two mechanisms of action that block the voltage-sensitive sodium channels to stabilize the excitability in the brain and control the seizure spread.

Drug Therapy for Parkinson's Disease:

Parkinsonism is a chronic, progressive, degenerative disorder of the central nervous system (CNS) characterized by resting tremor, bradykinesia, rigidity, and postural instability. Manifestations of Parkinson's disease also may occur with other CNS diseases, brain tumors, and head injuries. Drugs that deplete dopamine stores or block dopamine receptors, including the older antipsychotic drugs (phenothiazines and haloperidol), reserpine, and metoclopramide, can produce movement disorders such as secondary parkinsonism (which also involves extrapyramidal reactions. Treatment can be pharmacologic, nonpharmacologic, and/or surgical.

The first symptom of Parkinson's disease is often a resting tremor that begins in the fingers and thumb of one hand ("pill-rolling" movements.

Drugs Administered for the Treatment of Parkinson's Disease:

- **Dopamine receptor agonists:**
  1. **Levodopa,** the original prototype dopamine receptor precursor (prodrug), was developed in the 1960s. It is routinely administered with the drug **carbidopa**.
  2. **Levodopa–carbidopa** (Sinemet).
- **Amantadine hydrochloride** is an antiparkinsonian and antiviral agent. It increases the dopamine release in the nigrostriatal pathway of patients with Parkinson's disease.
- **Apomorphine hydrochloride** is an antiparkinsonian agent administered for "**off time**" episodes.
- **Bromocriptine mesylate** is an ergot derivative that directly stimulates dopamine receptors in the brain.

- **Catechol-o-methyltransferase Inhibitors:**

  Tolcapone is the prototype COMT inhibitor. COMT plays a role in the brain metabolism of dopamine and metabolizes approximately 10% of peripheral levodopa. By inhibiting COMT, tolcapone increases levels of dopamine in the brain and relieves symptoms more effectively and consistently.