

Benzodiazepines • Benzodiazepines are widely used as anxiolytic drugs. • They have replaced barbiturates and meprobamate for treating anxiety and insomnia, as they are safer and more effective. • Despite their common usage, benzodiazepines may not necessarily be the best choice for treating anxiety or insomnia. • Selective serotonin reuptake inhibitors (SSRIs), with anxiolytic action, are often preferred for many cases as antidepressants. • For insomnia, nonbenzodiazepine hypnotics and antihistamines may be preferable.

A. Mechanism of Action • Benzodiazepines target γ -aminobutyric acid (GABA_A) receptors. • The GABA_A receptors are composed of a combination of five α , β , and γ subunits that span the postsynaptic membrane. • GABA binding triggers the opening of the central ion channel, allowing chloride ions to pass through the pore. • The influx of chloride ions causes hyperpolarization of the neuron, decreasing neurotransmission by inhibiting action potentials. • Benzodiazepines modulate GABA effects by binding to a specific, high-affinity site distinct from the GABA-binding site. • Benzodiazepines increase the frequency of channel openings produced by GABA. • The binding of a benzodiazepine increases the affinity of GABA for its binding site, and vice versa. • The clinical effects of benzodiazepines correlate with their binding affinity for the GABA receptor-chloride ion channel complex.

B. Therapeutic Uses

- 1. Anxiety Disorders** • Benzodiazepines are effective for anxiety symptoms associated with panic disorder, generalized anxiety disorder (GAD), social anxiety disorder, performance anxiety, posttraumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), and phobias like fear of flying. • They are also useful to treat anxiety related to depression and schizophrenia and should be reserved for severe anxiety. • Due to their addiction potential, they should only be used for short periods. • Clonazepam, lorazepam, and diazepam (long-acting agents) are preferred for patients needing prolonged treatment. • Antianxiety effects are less subject to tolerance than their sedative and hypnotic effects. • Alprazolam is effective for short- and long-term treatment of panic disorders, though it may cause withdrawal reactions.
- 2. Sleep Disorders** • Few benzodiazepines are useful as hypnotics, decreasing sleep onset latency and increasing stage II non-rapid eye movement (REM) sleep. • Both REM sleep and slow-wave sleep are decreased. • Treatment for insomnia requires balancing bedtime sedation at bedtime with residual sedation ("hangover") after waking. • Temazepam (intermediate-acting) and triazolam (short-acting) are commonly prescribed. • Flurazepam (long-acting) is rarely used due to its extended half-life, which may cause daytime sedation and drug accumulation in the elderly. • Estazolam and quazepam are intermediate- and long-acting agents, respectively.
- 3. Amnesia** • Shorter-acting benzodiazepines are used as a premedication for anxiety-provoking unpleasant procedures like endoscopy, dental procedures, and angioplasty. • They cause conscious sedation, keeping patients receptive to instructions. • Midazolam is used to facilitate amnesia while causing sedation before anesthesia.
- 4. Seizures** • Clonazepam is sometimes used as adjunctive therapy for certain seizures. • Lorazepam and diazepam are the drugs of choice for treating status epilepticus.
- 5. Muscular Disorders** • Diazepam treats skeletal muscle spasms from muscle strain and treats spasticity caused by degenerative conditions like multiple sclerosis and cerebral palsy.

Adverse Effects

- 1. Drowsiness and confusion** are the most common side effects.
- 2. Ataxia** occurs at high doses and precludes activities requiring fine motor coordination, like driving.
- 3. Cognitive impairment** (decreased long-term recall and retention of

new knowledge) can occur. 4. Triazolam rapidly develops tolerance. 5. Alcohol and other CNS depressants enhance benzodiazepine sedative–hypnotic effects. 6. Benzodiazepines are less dangerous than older anxiolytic and hypnotic drugs, making overdose seldom lethal unless taken with other central depressants, such as alcohol.