

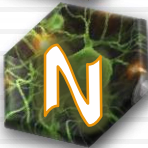


Lecture : 10

Anxiolytics (Antianxiety drugs)

Done by: Hossam alshehri

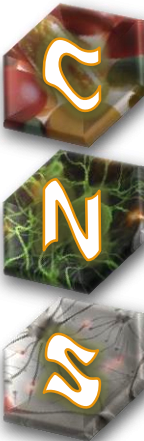
Revised by: Heba al-sherif & Noor alzahrani





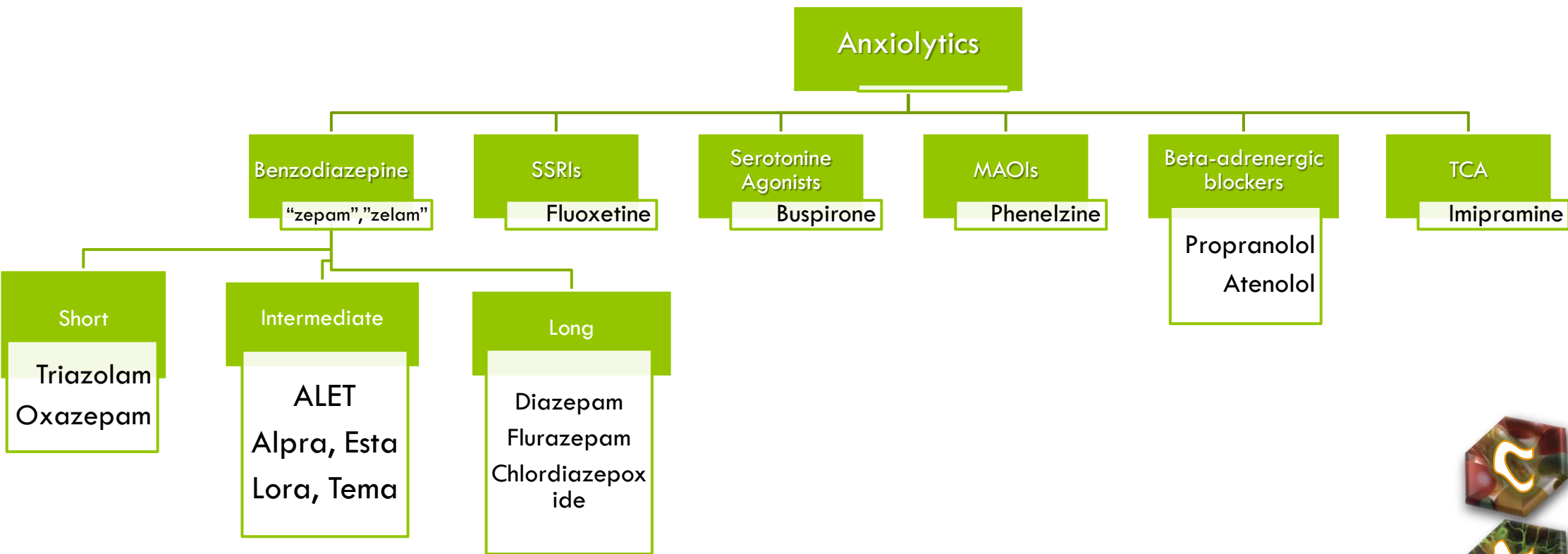
OBJECTIVES

- ❖ Define different types of anxiety disorders
- ❖ Classify types of drugs used for treatment of anxiety
- ❖ Recognize the different characteristics of antianxiety drugs





MIND MAP



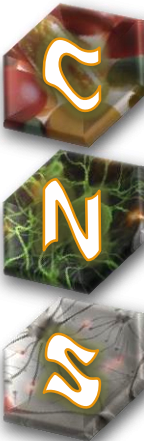


What is anxiety ?

- ❖ **Physical and emotional distress which interfere with normal life.**



- ❖ The effects of anxiety on performance can be shown on a curve. As the level of anxiety increases, performance efficiency increases proportionately, but only up to a point. As anxiety increases further, performance efficiency decreases. Before the peak of the curve, **anxiety is considered adaptive**, because it helps people prepare for a crisis and improve their functioning. Beyond the peak of the curve, anxiety is considered maladaptive, because it produces distress and impairs their functioning.





anxiety

Types of anxiety

- 1- Generalized anxiety disorder
- 2- Panic disorder
- 3- Phobia
- 4- Post traumatic stress disorder
- 5- Obsessive compulsive disorder

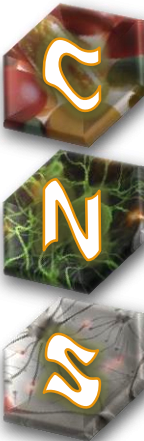
Symptoms

Emotional Symptoms of anxiety

- irrational and excessive fear and worry
- Irritability
- Restlessness
- Trouble concentrating
- Feeling tense

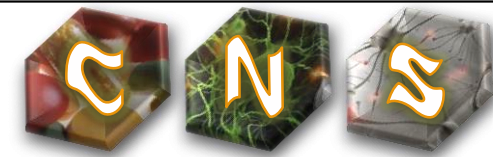
Physical Symptoms of Anxiety

- Sweating
- Tachycardia
- Shortness of breath
- Stomach upset
- Frequent urination or diarrhea
- Sleep disturbances (Insomnia)
- Fatigue





Types of anxiety



Types	definition
Generalized Anxiety Disorder	Patients are usually and constantly worried about health, money, work with no apparent reasons.
Obsessive-Compulsive Disorder (OCD)	An anxiety disorder in which people cannot prevent themselves from unwanted thoughts or behaviours that seem impossible to stop as washing their hands .
Post-traumatic stress disorder (PTSD)	An anxiety disorder that affects people who have experienced a severe emotional trauma, such as rape or dramatic car accident, or even war.
Panic disorder	An disorder in which people have sudden and intense attacks of anxiety in certain situations.
Phobia	An intense, uncontrolled fear of a specific situation such as open spaces & heights.

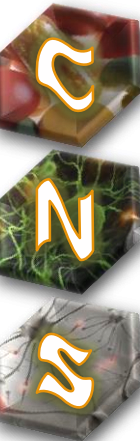


Treatment of anxiety

1-Psychotherapy

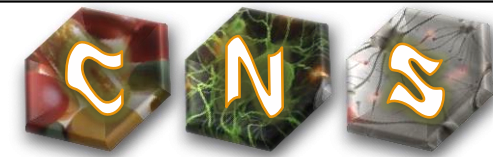
2-Anxiolytics

1. **Benzodiazepines (BDZ).**
2. **5HT_{1A} agonists.**
3. **5HT reuptake inhibitors.**
4. **Tricyclic Antidepressants**
5. **Beta-adrenergic blockers**
6. **MAO inhibitors**





Benzodiazepines



Mechanism of Action

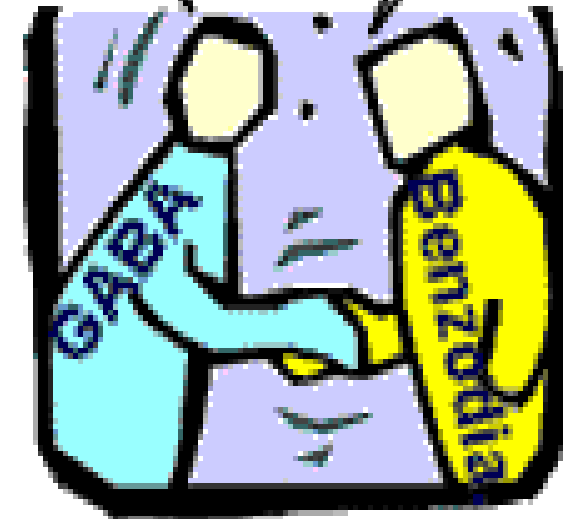
Benzodiazepines act By

binding to BZ receptors in the brain → enhance GABA action
in the brain

GABA is an inhibitory neurotransmitter

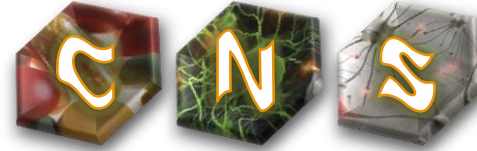
Enhancing the binding of GABA with Benzodiazepines can ease an anxious patient as a result of increased Cl⁻ influx

Let's reduce some brain activity!





Benzodiazepines

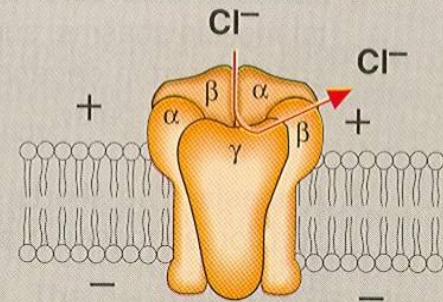


Closed Cl⁻ channel.
When there's no
GABA

GABA opens Cl⁻
channel

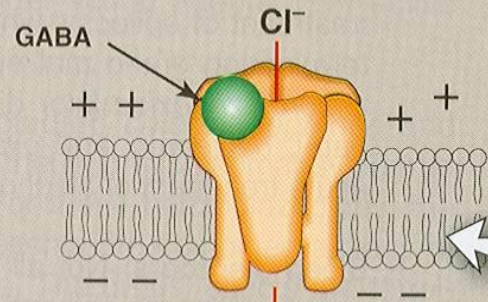
Benzodiazepine
enhance the binding
of GABA resulting in
greater Cl⁻ influx

A Receptor empty
(no agonists)



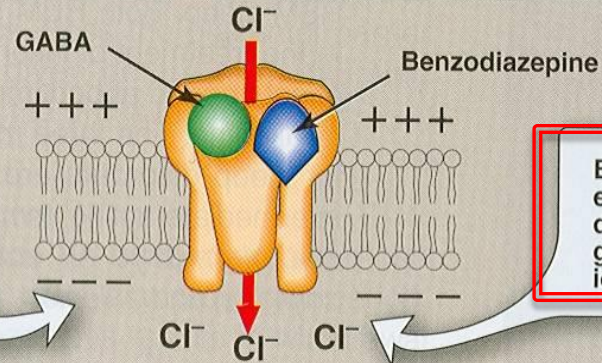
Empty receptor is inactive, and the coupled chloride channel is closed.

B Receptor binding GABA



Binding of GABA causes the chloride ion channel to open, leading to hyperpolarization of the cell.

C Receptor binding GABA and benzodiazepine

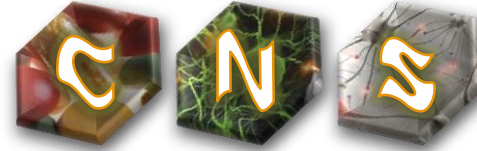


Entry of Cl⁻ hyperpolarizes the cell, making it more difficult to depolarize, and therefore reduces neural excitability.

Binding of GABA is enhanced by benzodiazepine, resulting in a greater entry of chloride ion.



Benzodiazepines



Can be classified according to the **duration of action** into **short, medium & long-acting**

★ Short-acting

★ 3-8 Hours

Oxazepam
Triazolam

★ Intermediate-acting

★ 10-20 Hours

Alprazolam
Estazolam
Lorazepam
Temazepam

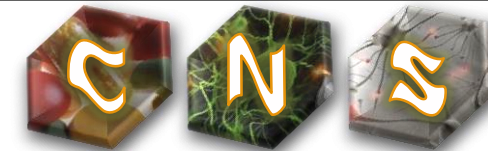
★ Long-acting

days
1-3

Clorazepate
Chlordiazepoxide
Diazepam
Flurazepam
Quazepam

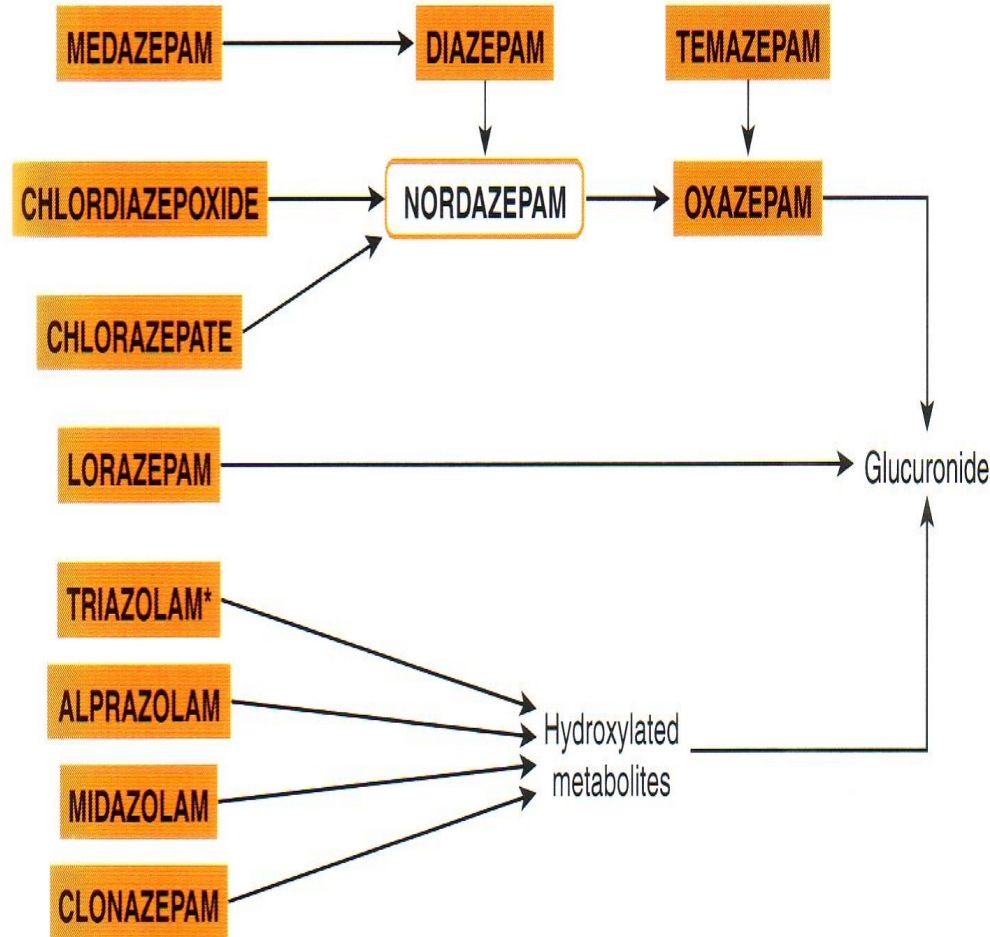


Benzodiazepines



Nordazepam has a long half-life

Lorazepam doesn't have an active metabolite, so it has short duration of action.

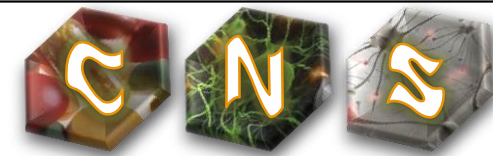


*Triazolam withdrawn in UK

Fig. 36.4 The metabolism of benzodiazepines. The N-demethylated metabolite nordazepam is formed from a number of benzodiazepines and is important because it is biologically active and has a very long half-life. Compounds with pharmacological activity are shown in blue. Drugs available for clinical use are shown in shaded boxes.



Benzodiazepines



Pharmacological Actions

- Anxiolytic action.
- Depression of cognitive and psychomotor function
- **Sedative & hypnotic actions**
- **Anterograde amnesia (not retrograde)**
- Minimal depressant effects on
 - ✓ Cardiovascular system
 - ✓ Respiratory system
- Some have **anticonvulsant effect:**
 - ✓ Clonazepam, diazepam.

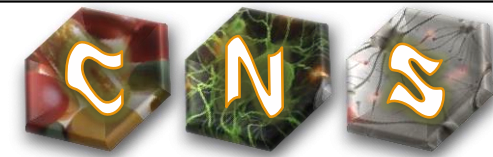
PHARMACOKINETICS

- are **lipid soluble**
- well absorbed **orally**,
- can be given parenterally
- **Chlordiazepoxide- Diazepam (IV only NOT IM)**
- widely distributed.
- **cross placental barrier (Fetal depression).**
- **excreted in milk (neonatal depression).**
- metabolized in the liver to active metabolites (long duration of action- cumulative effect).





Benzodiazepines



Therapeutic uses

☑ Anxiety disorders:

- Short term relief of severe anxiety
- General anxiety disorder
- Obsessive compulsive disorder
- Panic attack with depression
- Alprazolam (antidepressant effect)
- Benzodiazepines are fast acting—typically bringing relief within thirty minutes to an hour.

☑ Sleep disorders (Insomnia).

Triazolam short acting,

Lorazepam intermediate acting,

Flurazepam long acting

☑ Treatment of epilepsy

Diazepam

Lorazepam

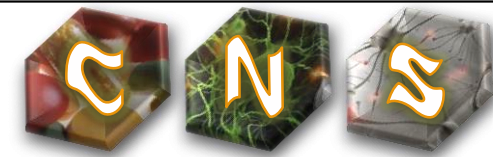
☑ In anesthesia

Preanesthetic medication (diazePam).

• Induction of anesthesia (Midazolam, IV)



Benzodiazepines



Adverse Effects

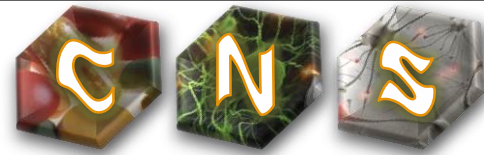
- **Ataxia (motor incoordination)**
- **Cognitive impairment.**
- **Impairment of driving ability**
- **Hangover: (drowsiness, confusion)**
- **Anterograde amnesia**
- **Tolerance & dependence**
- **Risk of withdrawal symptoms**
Rebound insomnia, anorexia, anxiety, agitation, tremors and convulsion.
- **Toxic effects: respiratory & cardiovascular depression in large doses.**
- **Psychological & physical dependence with continuous use.**

Precautions:

- **pregnant women or breast-feeding.**
- **Dose reduction is recommended in: Liver disease ,old people.**



Benzodiazepines



Drug interactions

	Examples
CNS depressants	<u>Alcohol & Antihistaminics</u> of ↑ effect of benzodiazepines
Cytochrome P450 (CYT P450) inhibitors	<u>Cimetidine & Erythromycin</u> ↑ $t_{1/2}$ of benzodiazepines
CYT P450 inducers	<u>Phenytoin & Rifampicin</u> ↓ $t_{1/2}$ of benzodiazepines

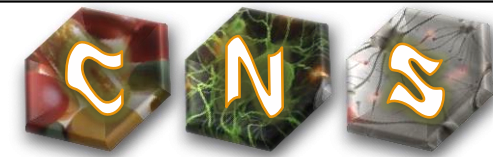
“CNS depressants” increase the effect of BDZ

“CYT P450 inhibitors” increase the half life of BDZ

“CYT 450 inducers” decrease the half life of BDZ



5HT_{1A} agonists



- Acts as agonist at brain 5HT_{1A} receptors
- Rapidly absorbed orally.
- T_{1/2} : (2 – 4 h). Slow onset of action.
- Liver dysfunction → ↓ its clearance. (because 5HT_{1A} agonists are metabolized in the liver)

Buspirone

- Only anxiolytic
- No hypnotic effect.
- Not muscle relaxant.
- Not anticonvulsant.
- No potentiation of other CNS depressants.
- Minimal psychomotor and cognitive dysfunctions.
- Does not affect driving skills.
- Minimal risk of dependence.
- No withdrawal signs.

Uses of buspirone

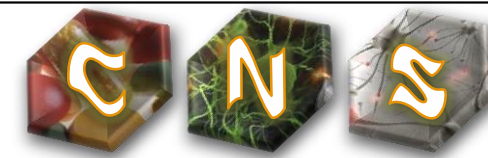
As anxiolytic in mild anxiety & generalized anxiety disorders.

Disadvantages of buspirone

- Slow onset of action (delayed effect)
- Not effective in severe anxiety/panic disorder.
- GIT upset, dizziness, drowsiness
- Drug Interactions with CYT P450 inducers and inhibitors



Beta Blockers

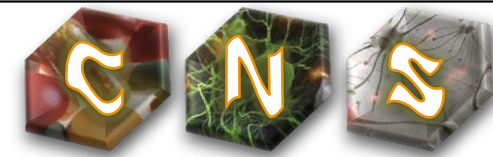


- **Propranolol – atenolol**
- Act by blocking peripheral sympathetic system.
- **Reduce somatic symptoms of anxiety.**
- **Decrease BP & slow HR.**
- Used in **performance anxiety (stage fright)**.
- Are **less effective** for other forms of anxiety.

CAUTIONS :
Asthmatic patients
Cardiac failure
Peripheral vascular diseases



Tricyclic Antidepressants



Doxepin- imipramine – desipramine

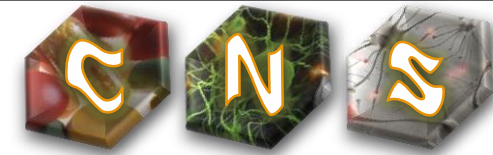
- Act by reducing uptake of 5HT & NA.
- Used for anxiety especially associated with depression.
- Effective for panic attacks.
- Delayed onset of action (weeks).

Side effects of tricyclic antidepressants

- Atropine like actions (dry mouth-blurred vision).
- α -blocking activity (Postural hypotension).
- Sexual dysfunction.
- Weight gain.



Selective serotonin reuptake inhibitors (SSRIs)



Fluoxetine

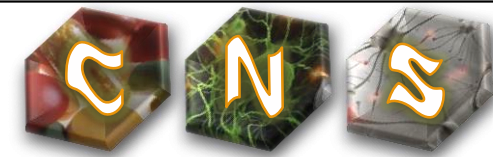
- acts by blocking uptake of 5HT
- Orally
- Delayed onset of action (weeks).
- Long half life
- Used as **FIRST LINE OF TREAT MOST ANXIETY DISORDERS** “panic disorder – OCD - Generalized anxiety disorders – phobia”

Side effects of SSRIs

- Nausea, diarrhea
- Weight gain or loss
- Sexual dysfunction
- Dry mouth
- Seizures
- Sleep disturbance



Monoamine oxidase inhibitors (MAOIs)



Phenelzine

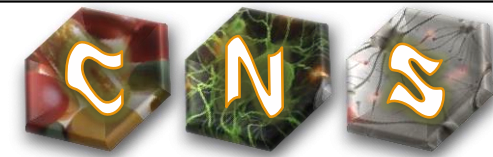
- act by **blocking** the action of **MAO enzymes**.
- **Used for panic attacks and phobia.**
- **Require dietary restriction**
- **Avoid** wine, beer, fermented foods as old cheese that contain **tyramine**.

Side effects

Dry mouth, constipation, diarrhea, restlessness, dizziness.



Synopsis Of Anxiolytics

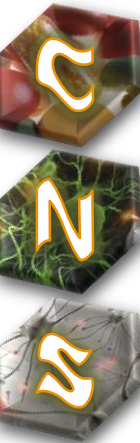


CLASSES OF ANXIOLYTICS	USES	Adverse effects
Benzodiazepines	Generalized anxiety disorders, OCD, phobia, panic attack	Ataxia, confusion, dependence, tolerance, withdrawal symptoms,
SSRIs (Fluoxetine)	Generalized anxiety disorders, OCD, phobia, panic attack	weight gain, sexual dysfunction Dry mouth
Tricyclic antidepressants (doxepin, imipramine)	anxiety with depression. panic attacks	weight gain, sexual dysfunction, atropine like actions
5HT1A agonists (Buspirone)	Mild anxiety Not effective in panic attack	Minimal adverse effects
Betablockers(propranolol,atenolol)	Phobia (social Phobia)	Hypotension
MAOIs (Phenelzine)	Used for panic attacks and phobia.	Dry mouth, constipation, diarrhea, restlessness, dizziness.



SUMMARY

1. BDZ act by binding to BZ receptors in the brain increase Cl⁻ influx
2. BDZ Can be classified according to the **duration of action** into **short, medium & long- acting**
3. Therapeutic uses of BDZ in **Anxiety disorders, Sleep disorders (Insomnia), Treatment of epilepsy, In anesthesia**
4. **5HT_{1A} agonists** Acts as agonist at brain 5HT_{1A} receptors
5. **Uses and disadvantages of buspirone**
6. **Beta Blockers**, Act by blocking peripheral sympathetic system. Used in **performance anxiety**
7. **Tricyclic Antidepressants** Act by **reducing uptake of 5HT & NA**, Side effects of tricyclic antidepressants.
8. **SSRIs** acts by blocking uptake of 5HT, Side effects of SSRIs
9. **MAOIs** act by **blocking** the action of **MAO enzymes**, Side effects





QUESTIONS

Q1/ Which of the following is a long acting BDZ and can be used to treat insomnia ?

- a/ diazepam
- b/ Triazolam
- c/ Flurazepam
- d/ chlordiazepoxide

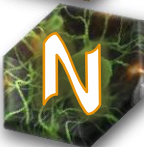
Q2/ a doctor subscribed diazepam to a patient who is taking erythromycin, which of the following statements is correct ?

- a/ the effect of diazepam will increase
- b/ the half life of diazepam will increase
- c/ the half life of diazepam will decrease
- d/ the effect of erythromycin will decrease

Q3\ Which one is used in social anxiety ?

- a\ Diazepam
- b\ Phenezine
- c\ Propranolol

Q1 /c
Q2/b
Q3\c





QUESTIONS

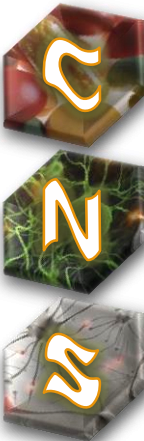
Q4\Which of them used for Anexiety with Depression ?

a\Alprazepam

b\imipramine

c\ a+b

Q4\c



THE END



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