

CENTRALLY ACTING MUSCLE RELAXANTS (spasmolytics)

Prepared By

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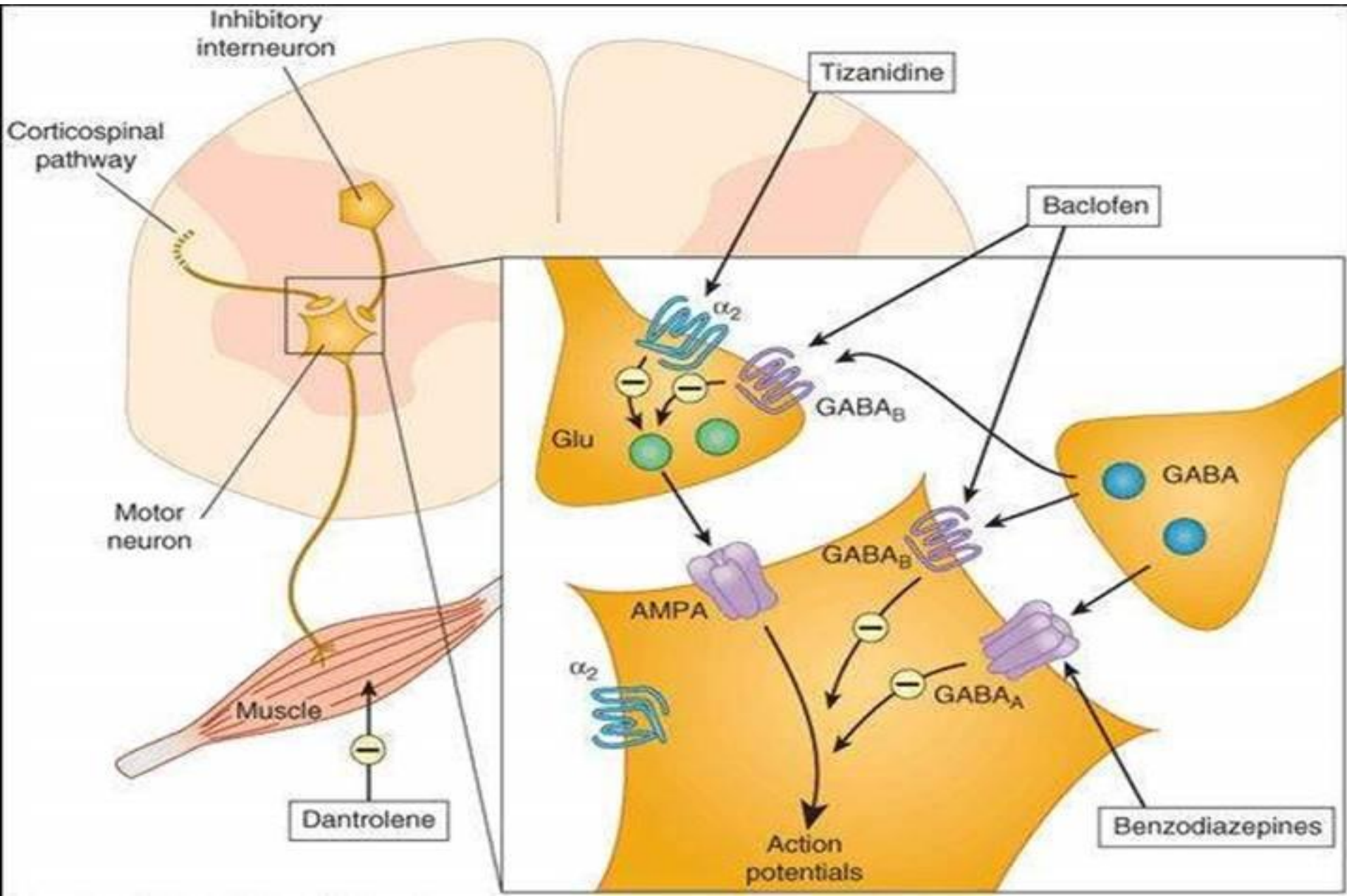
- **Muscle spasm: (spasm = involuntary muscular contractions)**
- Many diseases of the brain and spinal cord produce an increase in muscle tone, which can be painful and disabling.
- **Eg:** Spasticity resulting from birth injury or cerebrovascular disease, and the paralysis produced by spinal cord lesions.
- When the disease has progressed for some years it can cause muscle stiffness and spasms.
- **Other symptoms:**
- Pain, fatigue, difficulty passing urine and tremors.
- **Causes:**
- Local injury or inflammation can also cause muscle spasm, and chronic back pain is also often associated with local muscle spasm.

- **Centrally acting muscle relaxants: (spasmolytics)**
- These are the drugs that act centrally in cerebrospinal axis to reduce muscle tone and cause muscle paralysis.
- They depress spinal and supra-spinal reflexes.
- Postural control is usually lost by centrally acting muscle relaxants.
- Depresses CNS.
- Drowsiness and confusion are very common side effects of these agents. (due to poly synaptic reflex depression)

CLASSIFICATION

- GABA derivatives – Baclofen
- Benzodiazepines – Diazepam, Lorazepam, Clonazepam
- Central α_2 agonist – Tizanidine
- Mephenesin congeners – Mephenesin, Carisoprodol,
Methocarbamol
- Directly acting drug – Dantrolene
- Natural derivatives – Sativex, botulinum toxin
- Other drugs – Gabapentin, pregabalin, glycine

MECHANISM OF ACTIONS



- **BACLOFEN:** Baclofen is a selective agonist at GABAB.
- It is a chlorophenyl derivative of GABA.
- It is originally prepared as a lipophilic GABA-like agent in order to assist penetration of the blood–brain barrier, which is impermeable to GABA itself.
- The antispastic action of baclofen is exerted mainly on the spinal cord.
- **MOA:**
- It inhibits both monosynaptic and polysynaptic activation of motor neurons.
- It increases release of inhibitory neurotransmitter like GABA.
- It reduces release of glutamate.
- It is effective when given by mouth. **It is not useful in epilepsy.**
- Orally well absorbed and 35% excreted unchanged in urine. ($t_{1/2}$ - 3-4 hours)
- Given intrathecally too.
- **Use:** In the treatment of spasticity associated with multiple sclerosis or spinal injury.
- It is ineffective in cerebral spasticity (continuous muscle contractions) caused by birth injury.
- **ADRs:** Drowsiness, motor in-coordination, nausea, behavioral effects, tachycardia and seizures.

- **MEPHENESIN:** Acts on mid brain, thalamus and spinal cord.
- Does not block neuromuscular transmission. It is an NMDA receptor antagonist.
- **Uses:**
- Can control epileptic seizures within 30 sec.
- Has central sedative action. So useful in psychotic cases.
- Provides muscular relaxation and relief from tremors that occur in parkinsonism.
- **ADR:** Weakness, nystagmus (rapid eyeball movement), double vision, muscular in-coordination.
- **Dose:** 250 mg tablet; 0.5 – 3g IV injection.
- **Benzodiazepines:** They have anxiolytic effect too.
- Interacts with GABAA receptors and prevents binding of GABA at post synapse.
- They produce muscle relaxation by an effect in the spinal cord.

- **Tizanidine:**

- It is an α_2 -adrenoceptor agonist that relieves spasticity associated with multiple sclerosis and spinal cord injury.
- It inhibits release of excitatory neurotransmitters in spinal interneurons.
- It facilitates release of glycine (inhibitory neurotransmitter).
- **ADRs:** dry mouth, drowsiness, night time insomnia and hallucinations.

- **Sativex:**

- Past evidences suggested that smoking **cannabis** relieves the painful muscle spasms associated with multiple sclerosis.
- Sativex, a cannabis extract containing Δ^9 -tetrahydrocannabinol (also known as THC or dronabinol) and cannabidiol, is licensed in some countries as a treatment for spasticity in multiple sclerosis.
- It also has pain-relieving properties.

- **Dantrolene:**
- It acts peripherally rather than centrally to produce muscle relaxation.
- **Botulinum toxin:**
- It is injected into a muscle.
- This neurotoxin causes long-lasting paralysis confined to the site of injection.
- Its use to treat local muscle spasm is increasing.
- Its non-medicinal use as a 'beauty' treatment has become widespread.