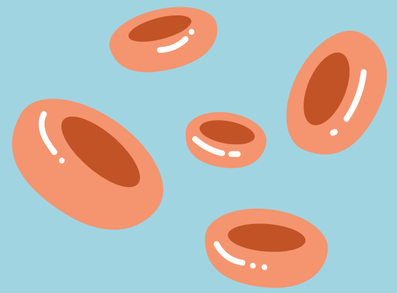
Xylazine

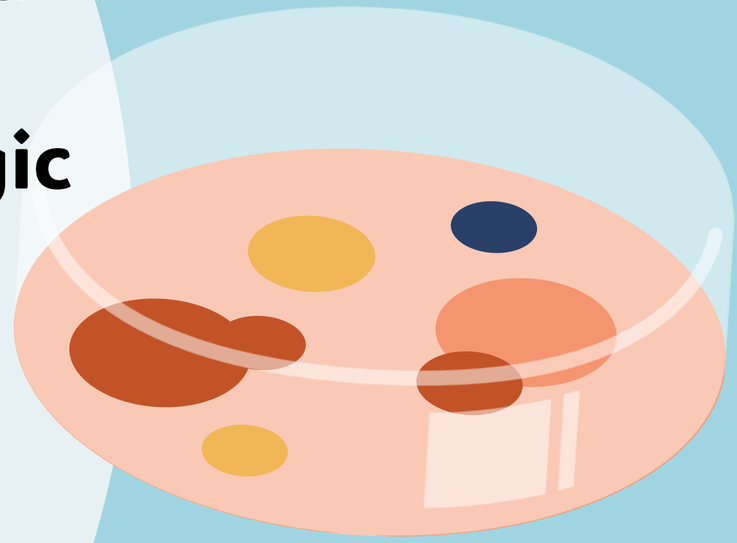
Assist. Lecturer Najwa Imad Sulaiman

Email: najwa_imad@tu.edu.iq



Introduction

Xylazine is a non-opioid sedative, analgesic, and muscle relaxant commonly used in veterinary medicine. It belongs to the class of α2-adrenergic agonists, similar to drugs like clonidine and dexmedetomidine. While primarily utilized for animal sedation and anesthesia, xylazine has gained attention due to its increasing misuse in humans, leading to significant public health concerns.



Chemical Structure and Mechanism of Action

Xylazine ($C_{12}H_{16}N_2S$) is a thiazine derivative that exerts its effects by stimulating α2-adrenergic receptors in the central and peripheral nervous systems. This action leads to a decrease in norepinephrine release, causing sedation, muscle relaxation, and analgesia.

Pharmacological effects

a. Analgesia.

b. Sedation: α2 -Agonists induce potent sedation High doses of α2-agonists may induce CNS excitation.

c. Skeletal muscle relaxation.

d. Emesis: It is induced in carnivores and omnivores cats, and less frequently in dogs.

e.GI effects: α2-Agonists reduce both GI motility and secretions.

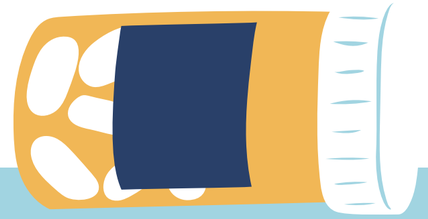
f. Cardiovascular effects: causes mild hypertension followed by hypotension.

g. Renal effects: α2-Agonists induce diuresis by inhibiting vasopressin release.

h. Respiratory effects: α2-Agonists cause hypoxemia (and sometimes pulmonary edema) in ruminants, especially sheep.

i. Neuroendocrine effects:

- α2-Agonists inhibit sympathoadrenal outflow and decrease the release of norepinephrine and epinephrine.
- α2-Agonists inhibit insulin release.
- α2-Agonists increase growth hormone release.



Pharmacokinetics

- **Absorption:** Rapidly absorbed following intramuscular (IM), intravenous (IV), or subcutaneous (SC) administration.
- **Distribution:** Widely distributed across tissues, with high lipid solubility.
- **Metabolism:** Primarily metabolized in the liver.
- **Excretion:** Excreted via urine and feces, with elimination half-life varying by species.

Veterinary Applications

Xylazine is extensively used in veterinary medicine for various purposes:

- **Sedation and anesthesia in large animals (horses, cattle, deer) and small animals (dogs, cats).**
- **Pre-anesthetic agent to reduce the required dose of general anesthetics.**
- **Analgesic for minor surgical and diagnostic procedures.**

Side Effects and Adverse Reactions

Although effective, xylazine can cause various side effects:

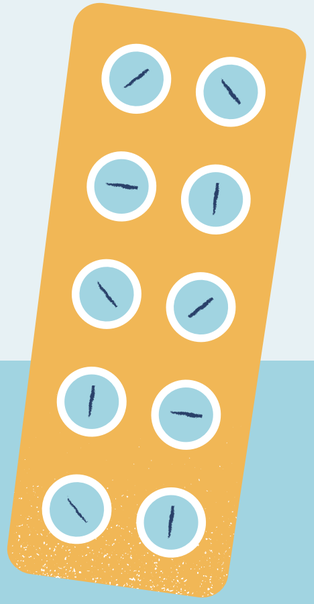
- Cardiovascular effects: Bradycardia, hypotension, arrhythmias.
- Respiratory depression: Dose-dependent decrease in respiratory rate.
- Gastrointestinal issues: Vomiting in cats and dogs, reduced gastrointestinal motility in ruminants.
- Hypothermia and hyperglycemia: Due to decreased metabolic rate and altered insulin response.

Human Misuse and Toxicity

Xylazine has emerged as a significant drug of abuse, often mixed with opioids like fentanyl ("tranq dope"). Its misuse leads to severe health risks, including:

- **CNS depression:** Sedation, disorientation, and unconsciousness.
- **Respiratory depression:** Potentially fatal, especially when combined with opioids.
- **Severe skin ulcerations and necrosis:** Linked to chronic use via injection.
- **Bradycardia and hypotension:** Requiring emergency medical intervention.

Treatment of Xylazine Overdose



There is no specific antidote for xylazine toxicity in humans. Management includes:

- **Supportive care:** Oxygen therapy, intravenous fluids, and airway management.
- **Reversal agents:** Atipamezole and yohimbine, α2-antagonists used in veterinary settings, may have potential benefits.

Contraindications

- Cardiac aberrations.
- Hypotension or shock.
- Renal insufficiency.
- Hepatic impairment.
- Epilepsy.
- The use of xylazine in combination with ketamine should be used only in young healthy animals because this combination synergistically suppresses the cardiopulmonary function of the animal.
- Immediate collapse, convulsions, and sudden death can occur in horses given xylazine into the carotid artery.
- A cautious approach should be taken whenever xylazine is used in the treatment of colic because xylazine's powerful analgesic effect can mask the underlying problem and because xylazine can paralyze the GI tract.
- Xylazine should not be given to animals (particularly mares and ruminants within the last month of pregnancy since it may induce abortion.
- Xylazine should not be given to dehydrated animals or those with urinary obstruction because of its potent diuretic effect.

Feature	Xylazine	Ketamine
Drug Class	α2-Adrenergic Agonist	Dissociative Anesthetic
Mechanism of Action	Sedation, analgesia, and muscle relaxation by reducing norepinephrine release.	Induces dissociative anesthesia by blocking NMDA receptors.
Primary Use	Sedation and pre-anesthesia in animals.	General anesthesia and induction.
Muscle Relaxation	Strong	Minimal
Analgesia	Moderate	Mild
Onset of Action	5–15 min (IM)	1–5 min (IM), <1 min (IV)
Duration of Action	30–60 min	10–30 min
Cardiovascular Effects	Bradycardia, hypotension.	Increased heart rate, hypertension.
Respiratory Effects	Depression	Mild depression, risk of apnea at high doses.
Reversal Agent	Atipamezole, Yohimbine.	No specific reversal agent.

"A Positive Attitude Causes a Chain Reaction of Positive Thoughts, Events and Outcomes. It is a Catalyst and it Sparks Extraordinary Results."

- Wade Boggs