

Interactions Between Behaviour Medications And Other Medications including general anaesthetic in small animals and equines

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Pharmacokinetics or Pharmacodynamics interactions

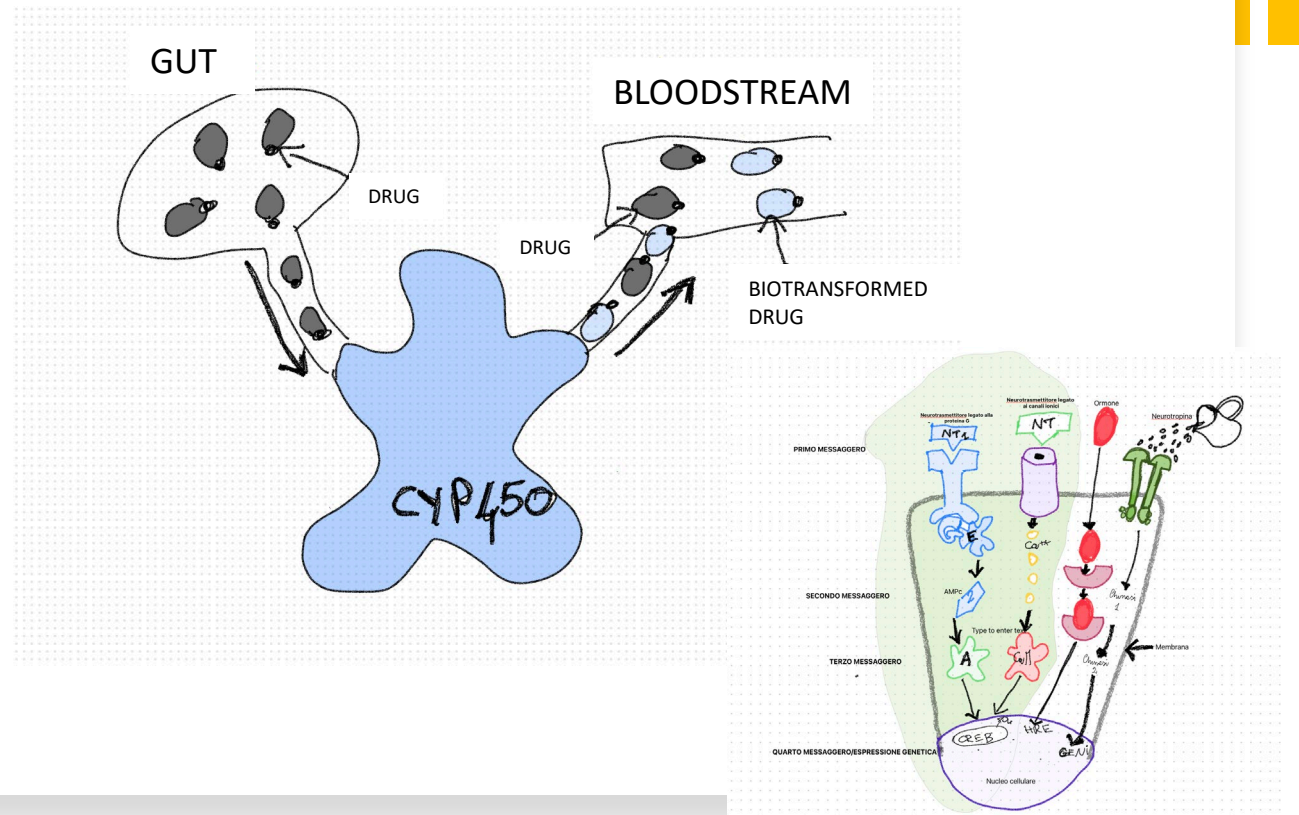
Drug-Drug Interaction

Pharmacokinetics

Absorption, distribution,
metabolization and excretion

Pharmacodynamics

Actions on receptor sites, ion
channels, enzymes



Serotonin syndrome

Rare event but not impossible

Happens when the concentration of serotonin reach toxic levels

- High BP, high HR
- > temperature
- Dilated pupils
- Tremors, incoordination
- Muscle twitching and rigidity

Can occur when other antidepressants are combined and there is an inhibition of neurotransmitter degradation (the synaptic cleft is flooded)

Avoid combining the following with a serotonergic medication:

- MAOIs (Selgian)
- Amitraz (Preventic, Mitaban)
- Supplements with tryptophan
- Herbal medications (St. John's Wort)

Trazodone and Tramadol present mild risk

General anesthesia and surgery risks in dogs and cats in treatment with psychotropic medications

SSRIs

- Increased risk of hypotension and respiratory depression
- Increased risk of bleeding
- Potential risk of serotonergic syndrome with some opioids

Trazodone

- Risk of hypotension and respiratory depression (reported similar to ACP in dogs)
- Potential risk of serotonergic syndrome with some opioids

IMAOs

- Increased risk of Serotonergic syndrome when used with opioids
- In general discontinuation two weeks before surgery is advised

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SSRIs

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Psychotropic medications and intra and perioperative analgesia

Analgesics	SSRIs, TCAs,	Trazodone	MAOIs
Morphine, codeine, buprenorphine, oxymorphone, hydromorphone, oxycodone	Low risk (risk of decreased analgesic effect of Codeine)	Low risk	Use with caution
Fentanyl, tapentadol, methadone	Medium risk – use with care	Medium risk	Increased risk of serotonin syndrome
Tramadol, pethidine , dextromethorphan	Increased risk of serotonin syndrome	Increased risk of serotonin syndrome	Contraindicated

Psychotropic medications, general anesthesia and surgery risks

Intra and perioperative risks	SSRIs	TCA	Trazodone	MAOIs
Medetomidine	Low risk (α -2 receptor agonist reduce serotonin excess)	Low-medium risk Increased risk of perioperative cardiac arrhythmias	Low risk	Low risk?
Propofol	Low-medium risk (propofol can increase dopamine and serotonin in the cortex)		Low risk (seems safe and Propofol dose necessary for induction reduced)	Low risk
Volatile anesthetic agents			Low risk/Safe	Medium risk Can increase hypothermic response Discontinue 2 weeks before surgery
Ketamine	Low risk Paroxetine, sertraline, fluoxetine, and fluvoxamine are inhibitors of the same liver CYT3A4: may > bioavailability of ketamine	Medium risk (possible additional sympathetic stimulation)	Low risk	Medium risk (Ketamine has indirect sympathomimetic effects with >BP and >HR) Discontinue 2 weeks before surgery
Bleeding risks	Low-medium risk – advised caution/control bleeding (alterations of platelet serotonin levels)			

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Equine psychopharmaceuticals and interactions with other medications



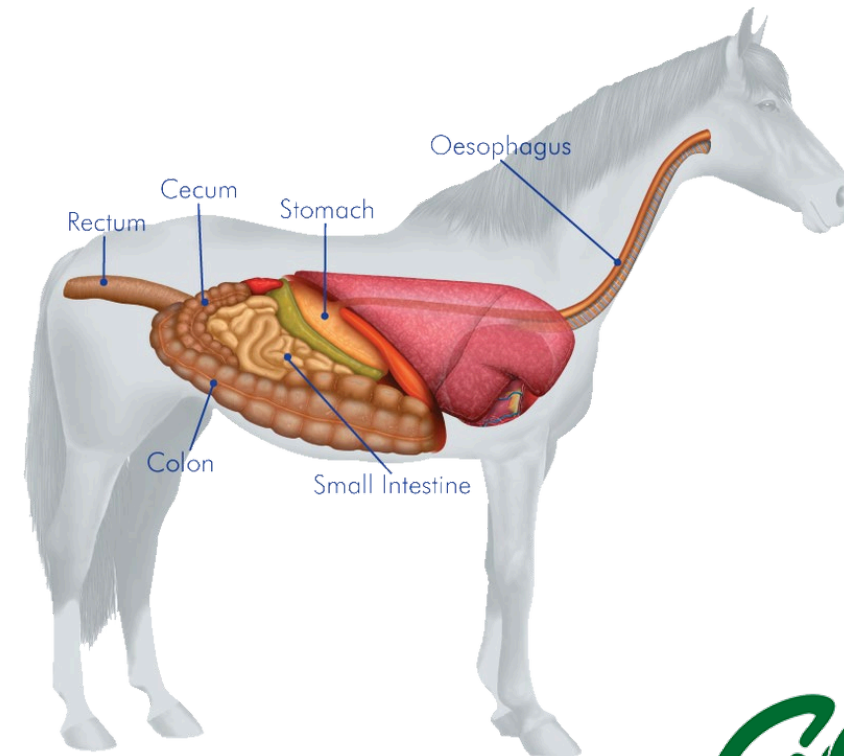
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THE UNIVERSITY of EDINBURGH
The Royal (Dick) School
of Veterinary Studies

Equine Psychopharmaceuticals

- Very limited publications
- Less experience with use
- Therefore less confidence in knowledge base
- Individual variability to response
- Bioavailability in horses is significant
 - Stomach – up to 15 litres (16hrs fasting to empty)
 - Small intestine – 70 litres
 - Cecum – 35 litres
 - Large intestine – 90 litres



Equine Psychopharmaceuticals

- Serotonin syndrome – not reported **yet** in horses
- Therefore unsure how similar clinical signs may be



Competition Regulations



Gabapentin

Pharmacokinetic profile and behavioral effects of gabapentin in the horse

- BEVA CAT suggest 120mg/kg effective dose
- 16% oral bioavailability
- Sedation at higher doses, ? Cumulative effect
- Study
 - No cardiovascular effects
- No concerns about interactions with commonly used medications in horses

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STANDARD ARTICLE

Journal of Veterinary Internal Medicine **ACVIM**
American College of Veterinary Internal Medicine
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Plasma disposition of gabapentin after the intragastric administration of escalating doses to adult horses



Fluoxetine (SSRI)

- Dose = 0.25mg/kg, low compared to other species
- Commonly used with other medications
- No concerns regarding general anaesthesia

Serotonin syndrome

- Have used successfully with low dose Trazodone
- Theoretical increased risk with metoclopramide or supplements high in L-tryptophan or St Johns Wort
- No other SSRI's that are published in horses



Amitriptyline (tricyclic antidepressant)

- Study
 - Reduced HR and borborygmi but still within normal reference ranges
- Have combined with low dose Trazodone



ORIGINAL PAPER | REVIEW ARTICLE | LETTER TO THE EDITOR

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SHORT COMMUNICATION

JOURNAL OF
Veterinary Pharmacology and Therapeutics WILEY


Pharmacokinetic study of oral amitriptyline in horses

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María José Estradé³ | Gonzalo Suarez¹ | Nadia Crosignani¹ 



Trazodone (serotonin antagonist/reuptake inhibitor)

Pharmacokinetics, pharmacodynamics and clinical use of trazodone and its active metabolite *m*-chlorophenylpiperazine in the horse

J. L. Davis¹  | J. Schirmer² | E. Medlin²

Investigation of the effects of orally administered trazodone on intraocular pressure, pupil diameter, physical examination variables, and sedation level in healthy equids

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Rachel C. Hector DVM, MS
Kathryn L. Wotman DVM

OBJECTIVE
To investigate the effects of orally administered trazodone on intraocular pressure (IOP), pupil diameter measured in the vertical plane (ie, vertical pupil diameter [VPD]), selected physical examination variables, and sedation level in healthy equids.

Pharmacokinetics and selected pharmacodynamics of trazodone following intravenous and oral administration to horses undergoing fitness training

- Commonly used
- Combined with Fluoxetine or Amitriptyline starting with low doses
- Combined with alpha 2 and butorphanol with no issues
- Acts synergistically with Alprazolam and ACP
- Study
 - Hypotension
 - Intraocular pressure was lower for same time period
 - Vertical pupil diameter reduced at 30mins
 - Mean rectal temperature reduced 1-8hrs



Alprazolam (benzodiazepine)

- Potent anxiolytic
- Beware ataxia/muscle weakness – cumulative effect
- Has been used to GA a single case - ? Use of diazepam on induction

JOURNAL OF
Veterinary Pharmacology and Therapeutics
J. vet. Pharmacol. Therap. 38, 301–304. doi: 10.1111/jvp.12192. SHORT COMMUNICATION

Pharmacokinetics and physiologic effects of alprazolam after a single oral dose in healthy mares

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Wong, D. M., Davis, J. L., Alcott, C. J., Hepworth-Warren, K. L., Galow-Kersh, N. L., Rice, S., Coetzee, J. F. Pharmacokinetics and physiologic effects of alprazolam after a single oral dose in healthy mares. J. vet. Pharmacol. Therap. 38, 301–304.



Questions?



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