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**CORRESPONDING AUTHOR**

**Federica Di Cesare**
federica.dicesare@unimi.it

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UNIVERSITÀ DEGLI STUDI DI MILANO
DIPARTIMENTO DI SCIENZE VETERINARIE PER LA SALUTE, LA PRODUZIONE ANIMALE E LA SICUREZZA ALIMENTARE

# Pharmacokinetics of dexmedetomidine combined with methadone following oral-transmucosal and intramuscular administration in dogs

Federica Di Cesare[1*], Petra Cagnardi[1], Daniela Gioeni[2], Elisa S. D'Urso[2], Vanessa Rabbogliatti[2], Lorena Lucatello[3], Roberta Merlanti[3], Giuliano Ravasio[2], Roberto Villa[1]

[1] *University of Milan, Department of Health, Animal Science and Food Safety, Italy*

[2] *University of Milan, Department of Veterinary Medicine, Italy*

[3] *University of Padua, Department of Comparative Biomedicine and Food Science, Italy*

## Abstract

Oral-transmucosal (OTM) drug delivery refers to noninvasive and painless administration of medical preparations through any oral cavity membrane to achieve systemic effects (Sattar *et al.*, 2014). Regarding sedative drugs, OTM administration is very attractive in veterinary medicine, especially for patients difficult to inject and restrain (Messenger *et al.*, 2016). This study aims to compare the pharmacokinetics of dexmedetomidine after OTM and intramuscular (IM) administration combined with methadone. After obtaining Ethical Committee approval and owner's written consent, eight dogs, were administered with dexmedetomidine (10 µg/kg) and methadone (0.4 mg/kg) by OTM and other 4 dogs by IM route. Blood samples were collected at prefixed times up to four hours. Dexmedetomidine was quantified by a validated HPLC-MS method. On dexmedetomidine concentrations, a pharmacokinetic analysis was carried out with a noncompartmental approach (Phoenix WinNonlin® 7.0, Pharsight, Cary, NC). Mean ± SD terminal half-lives of dexmedetomidine were 187.42 ± 109.66 and 94.78 ± 34.08 min after OTM and IM administration, respectively. Maximum serum (Cmax) concentrations were 0.83 ± 0.32 and 9.09 ± 2.46 ng/mL for OTM and IM administration, respectively. Time to maximum concentration (Tmax) were 44.38 ± 32.16 and 21.25±11.39 min by OTM and IM administration, respectively. Area under the curve from 0 to the last measured concentration (AUClast) were 103.75 ± 30.23 and 614.87 ± 77.15 min*ng/mL for OTM and IM administration, respectively. Cmax, Tmax and AUClast values by OTM route demonstrate a lower and delayed absorption of the drug compared to IM. To complete the study, the pharmacokinetic analysis of methadone is foreseen, so as a clinical trial to compare the clinical effects of the combination of dexmedetomidine and methadone by OTM and IM administration and to establish an effective dosage of oral-transumucosal route in dogs for this association.

## References

*Messenger, K., M., Hopfensperger, M., Knych, H., K., Papich, M., G., 2016. Pharmacokinetics of detomidine following intravenous or oral-transmucosal administration and sedative effects of the oral-transmucosal treatment in dogs. American Journal of Veterinary Research. 77, 413-420.*

*Sattar, M., Sayed, O., M., Lane, M., E., 2014. Oral transmucosal drug delivery – Current status and future prospects. International Journal of Pharmaceutics. 471, 498-506.*





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