Cyclodextrins in veterinary use
What are cyclodextrins (CDs)?

- Composed of sugars
- Cyclic molecules
- Naturally occurring compounds
- Used in food, pharmaceuticals, drug delivery, chemical industries, agriculture, etc.
Why use cyclodextrins?

- Significant solubility enhancement
- Improvement of chemical stability
- Increased bioavailability, facilitated delivery
- Reduced aggregation
- Moderated irritation or reduced side-effects
- Maximized safety, complete renal elimination
- Enables formulation of water-insoluble APIs in all dosage forms
- Lower API doses can be achieved
- Potential antidote for organophosphate poisonings
**Who we are and what can we offer?**

CycloLab is the world's only all-around Cyclodextrin Service Provider

Our services include:

- Supplying cyclodextrins for commercial products and product development
- Screening cyclodextrin derivatives to find the right candidate for target API.
- Providing formulation development services, composition optimization, stability assessment.
- Offering analytical services to characterize complexes and products.
- Preparing pilot-scale amounts for cyclodextrin-API complexes under GMP for development purposes.
- Assisting in compilation of regulatory documentation.

For more information please click [here](#)
What is CycloLab?

Early phase drug development

IP services & consultancy

Analytical services

GMP synthesis and production
Antifungal agents

- **Voriconazole** is an antifungal drug for both human and veterinary use. In the formulation, *sulfobutyl-ether-beta-cyclodextrin (Dexolve™)* is used as an excipient.

- **Itraconazole** (Itrafungol™), it is used as antifungal drug in cats. In the formulation, *(2-hydroxypropyl)-beta-cyclodextrin* is used as an excipient.
Drugs affecting the cardiovascular system

- **Amiodarone** is an antihyarrythmic drug. It has several indications, and it is used in humans and in veterinary medication.
  - A new formulation (Nexterone™, PM101) contains *sulfobutyl-ether-beta-cyclodextrin* as a solubilizing agent instead of Polysorbate 80.
    - Does not cause hypotension
    - Safe for bolus administration
    - Plastic-friendly allows for prefilled non-glass syringes in future
    - Currently FDA-approved only in glass syringe

- **Pimobendan** (Vetmedin™), is a calcium sensitizer and a selective inhibitor of phosphodiesterase 3 (PDE3) with positive inotropic and vasodilator effects, used for the treatment of heart failure in dogs.
  - A new patent by Boehringer Ingelheim describes a formulation that consists of modified *cyclodextrins¹*.

¹ Boehringer Ingelheim Vetmedica GmbH, Liquid preparation comprising pimobendan, 2015, US9107952 B2
• **Maropitant** (Cerenia™), a drug used for the treatment of motion sickness and vomiting in dogs.

• In the formulation, *sulfobutyl-ether-beta-cyclodextrin* is used as a solubilizing agent.

• **Flubendazole** is an antihelmintic drug, used both in veterinary and human medication.

• *(2-hydroxypropyl)-beta-cyclodextrin* can be used as a solubilizing agent, to improve water solubility\(^2\).
• **Alfaxalone** (Alfaxan™), is a neuroactive steroid molecule with general anesthetic effects. It is used only in veterinary practice.
• In the formulation, (2-hydroxypropyl)-beta-cyclodextrin is used as a solubilizing agent.
Cyclodextrins are also used in vaccines

As an excipient, (2-hydroxypropyl)-beta-cyclodextrin is used.

- Suvaxyn PCV™ contains inactivated recombinant Porcine Circovirus type 1, expressing the Porcine Circovirus type 2 ORF2 protein. This vaccine is used for the active immunization of pigs over the age of 3 weeks against Porcine Circovirus type 2 (PCV2)
- Sulfolipo-cyclodextrin (SLCD) is used as an adjuvant
Essential oils and cyclodextrins

Several patents are about essential oil formulations with cyclodextrins, e.g.:

- Camphor oil (-respiratory stimulant)
- Lemon oil (-flavor enhancer)
- Cinnamon oil (-flavor enhancer)
- Garlic oil (-antimicrobial)

Vitamins and cyclodextrins

- \(\beta\)-cyclodextrins improve pharmacokinetics of \(\alpha\)-tocopherol in heifers
- Cyclodextrin encapsulated vitamin K (K\(_1\), K\(_2\)) can reduce osteochondral effects in animals

Cryopreservation

- Cholesterol-loaded cyclodextrins can prevent cryosurvival of animal sperms
- Cholestanol-loaded cyclodextrins improve quality of stallion spermatozoa

Effects of cyclodextrin complexes on methane production in heifers

- The \(\beta\)-cyclodextrin complex with guest materials appears to be a promising solution to mitigate methane emissions without reducing energy intake.

3 Bontempo V. et al. Kinetic behavior of three preparations of \(\alpha\)-tocopherol after oral administration to postpubertal heifers, American Journal of Veterinary Research, 2000, 61(5):589-93
4 Nbffin JR and Regtop H, Method for increasing bone density and/or reducing any osteochondral defects in an animal and a composition including vitamin K, 2015, US 8999962 B2
6 https://www.drugs.com/vet/camphor-injection-can.html
8 Chuaychu-Noo N et al., Supplementing rooster sperm with Cholesterol-Loaded-Cyclodextrin improves fertility after cryopreservation, Cryobiology, 2017, 74:8-12
9 Moraes EA et al., Cholestanol-loaded-cyclodextrin improves the quality of stallion spermatozoa after cryopreservation, Animal Reproduction Science, 2015, 158:19-24
10 Rajaraman B et al., Effects of caprylic acid and \(\beta\)-cyclodextrin complexes on digestibility, energy balance, and methane production in Korean Hanwoo heifers, Animal Feed Science and Technology, 2017, 234:72-77
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