



Specialist information

**from the Committee for Anaesthesia (GV-SOLAS)
in collaboration with Working Group 4 of the TVT**

The use of α -chloralose in experiments with rodents and rabbits

March 2016

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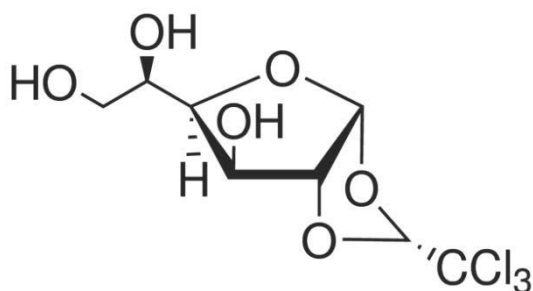
α -Chloralose, chloralose

Other names:

- 1,2-O-(2,2,2-Trichloroethylidene)- α -D-glucofuranose
- Anhydro-D-glucochloral
- Chloralose

Chemical formula: $C_8H_{11}Cl_3O_6$

EU hazard classification: harmful to health (harmful if swallowed, harmful if inhaled)



General information and structural formula from <http://www.vetpharm.uzh.ch/> and <https://en.wikipedia.org/wiki/Chloralose>

The following information has been collated from the wide-ranging literature (see literature list). The experiences of the authors and personal reports have been taken into account in the statement.

- A mixture of α -chloralose and β -chloralose (α -isomer, β -isomer) is generally called "chloralose".
- α -Chloralose is the substance with an anaesthetic effect.
- β -Chloralose is not considered to have any anaesthetic effect but does have toxic and convulsive effects.
- Only α -chloralose may be used for the anaesthesia of laboratory animals under certain conditions.

Historical background and use

The effects were described by Hanriot and other authors in 1893-97.

Plays no role in human medicine or veterinary practice. Not currently approved as a veterinary medicine in Germany.

Used as avicide and rodenticide for pest control. Since chloralose causes a sharp decrease in body temperature in small animals, it is used in the form of bait (mixed with meal or grain) mainly during the cold season (less than 15°C). Poisoned animals may be eaten by dogs and cats.

Prior use in laboratory animals

α -Chloralose has long been used in laboratory animals, mainly in physiological experiments studying the neuronal control of circulation and respiration. Since many autonomous reflexes remain intact, it is also used for other prolonged neuroscientific measurements, as well as magnetic resonance imaging in rare instances.

Practical application: Preparation, storage, properties of injection solution, route of administration

- Chloral derivative of pentose or hexose (chloral = chloral hydrate)
- Preparation: condensation of glucose, dry mass + chloral + sulphuric acid (Heffer 1889) produces a mixture of α - and β -chloralose.
- Only the alpha isomer, i.e., α -chloralose is effective as an anaesthetic. The anaesthetic potential of α -chloralose is 25 times greater than that of β -chloralose.
- It is assumed that the beta isomer - β -chloralose – has substantial toxic potential and can trigger convulsions.
- Metabolism: chloral $\rightarrow$ trichloroethanol
- α -Chloralose is obtainable as a white, crystalline powder. The powder is poorly soluble in water; usually, a 1% injection solution is prepared. Before use, the injection solution must be freshly prepared by dissolving in a heated (50-60°C) aqueous medium (e.g. isotonic saline solution). According to the literature, 25% urethane or 10% polyethylene glycol may also be added for better solubility (Green 1979, Fish et al. 2008). Cooling before injection, leaving the injection solution to stand for a long time or cooling it too much results in precipitation.
- After i.p. injection of α -chloralose, inflammatory reactions may occur and a slow onset of effect accompanied by side effects – depending on the animal species – can be expected.
- α -Chloralose should be administered i.v. as far as possible (Erhardt et al. 2012, Fish et al. 2008).
- After i.v. injection of α -chloralose, it takes at least 15 minutes until the onset of effect. For this reason, α -chloralose is frequently combined with other substances, such as morphine, barbiturates or urethane, especially during induction.
- Anaesthesia lasting 8-10 hours can be induced with α -chloralose; anaesthesia lasting several hours is also possible with a bolus i.v. injection.

Characterization of the anaesthetic: properties and side effects of anaesthesia

- Depression: sedation, general anaesthesia.
- Stimulation: myoclonic movements, generalized clonic movements
- No effect on cardiovascular and respiratory reflexes
- Hyperexcitability to stimuli (noises, tactile stimuli)

- Combination with other medicines to reduce hyperexcitability and convulsions.
- Probably only very slight if any analgesic potential.

Summary and opinion

A mixture with unknown or low proportions of α -chloralose that is named “chloralose” and not defined in any further detail must not be administered to animals for anaesthesia.

α -Chloralose is (to the authors' knowledge) not approved as a medicinal product. The absence of any ready-for-use formulations means that injection solutions must be prepared in the laboratory, posing an increased risk in its use. Aside from the potential risk to staff, considerable uncertainties for the anaesthesia and risks to the laboratory animal may arise as a result of errors or inattention in the preparation of the injection solution (e.g., with regard to concentration, solvent, solubility, especially precipitation or too high a temperature, and contaminations, etc.).

In view of the properties and effects of α -chloralose, the substance may only be used for experiments in which any alternatives and/or other agents cannot be used without making the study and/or study objective unattainable.

If the use of α -chloralose cannot be replaced by alternatives, it may only be used in non-recovery experiments (death under anaesthesia without recovery of consciousness, acute experiment, terminal experiment, final study). In this case, the combination of α -chloralose with other substances (e.g., fast-acting anaesthetics, analgesics) is advisable, especially during the induction of anaesthesia, to optimize the desired effects and reduce adverse effects and disadvantages.

The properties and mechanism of action of α -chloralose mean that only i.p. or i.v. injections are effective. The intravenous route (bolus, infusion) is the preferred option here, while i.p. injection should be avoided as far as possible.

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