

Atropine Supplement

How Made:

Atropine is a naturally occurring alkaloid of "*atropa belladonna*" (a plant also known as Deadly Nightshade). Extraction and processing racemize the alkaloid.

The main ingredient in Atropine solutions for injection, manufactured by Abbott, is atropine sulfate in injection solution. Along with water, most atropine injections also have two other excipients. These include an osmotically active isotonic saline 0.9% solution and benzol alcohol, a preservative. The injections doses of atropine are 0.4 mg/mL and 1.0mg/mL. For each injection type, the same concentration of isotonic saline 0.9%, and benzol alcohol, 0.015mg/mL are added. The pH of atropine solutions for injection should range between 3.0 and 6.5. Sulfuric acid is added to the solutions if pH adjustments are necessary.(Phone Interview, 2002b)

Pharmaceutical Uses and Mode of Action of Atropine in livestock:

Nerve impulses are transmitted to muscles and glands throughout the body by the action of specialized, naturally occurring chemicals known as neurotransmitters. Atropine blocks the ability of the neurotransmitter acetylcholine to stimulate certain muscles and glands. This produces effects ranging from drying of secretions (saliva, perspiration) to changing the size of the pupils and relief of intestinal muscle spasms.¹

In general, atropine administration dries up secretions in bronchial airways and helps reduce bronchial secretions. Atropine also helps reduce gastric secretions in ulcers. It relieves spasms in the intestinal tract as well as reduces bladder contractions.

Atropine is used in livestock in the following ways:

1. *Preanesthetic to prevent or reduce secretions of the respiratory tract*

Because of a lack of extended efficacy and potential adverse reactions, atropine is not used routinely as a preoperative agent in ruminants. If it is desired for use, a dose of 0.06- 0.12 mg/kg IM has been suggested. (Thurmon and Benson 1986)

2. *Treatment of sinus bradycardia, sinoatrial arrest, incomplete atrioventricular block*

Atropine can also reduce the arrhythmogenic effect of epinephrine.

3. *As an antidote for overdoses of cholinergic agents (e.g. physostigmine, etc.)*

4. *As an antidote for organophosphate or muscarinic mushroom intoxication*

In organophosphate poisoning, atropine is the antidote of choice approximately 95% of the time. Cattle treated with atropine for organophosphate poisoning are usually dosed for several days (usually more than 3 days) to counteract the effects of the poison as it takes several days for it to be completely excreted. Monitoring of the animal during treatment² of its heart rate, salivation and pupillary dilation ensures proper treatment protocols. Frequent dosing of atropine can be adjusted based on the above symptoms

¹*Atropine Sulfate Oral*

http://www.wholehealthmd.com/refshelf/drugs_view/0.1524.43.00.html#How_It_Works

² Dosage given: a) Approximately 1 mg/kg given to effect IV (use mydriasis and absence of salivation as therapy endpoints), may repeat every 1.5 – 2 hours as required subcutaneously (Oehme 1987) or 0.5 mg/kg (average dose); give ¼ of the dose IV and the remainder SC or IM; may repeat every 3 -4 hours for 1-2 days (Bailey 1986), b) 0.22 mg/kg, 1/4 of the dose administered IV and the remainder SC or IM (Package Insert; Atropine Injectable, L.A. – Fort Dodge; Post and Keller 2000)

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which is usually given at 3 to 6 hour intervals because of competition with acetylcholine.(Phone Interview, 2002a; Entriken, 2001; Phone Interview, 2002a)

5. *As an antidote for Larkspur poisoning from the Larkspur plant found mostly in western areas like Oregon and Washington where the cows accidentally eat that plant.*

6. *Hypersialism (Drooling, Ptyalism)*

Nerve impulses are transmitted to muscles and glands throughout the body by the action of specialized, naturally occurring chemicals known as neurotransmitters. Atropine blocks the ability of the neurotransmitter acetylcholine to stimulate certain muscles and glands.

7. *Treatment of bronchoconstrictive disease*

The dose needed for bronchodilation is 5 mg IV for a 400-500 kg animal (Beech 1987)

8. *Treatment of digestive tract disorders such as diarrhea in calves, pigs and lambs.*

A side effect of the use of atropine in cattle may result in loss of appetite and rumen stasis which may persist for several days.

9. *It is used in combination with a steroid in order to reduce inflammation in horses.*

For cattle, the dosage needed for adjunctive treatment of bovine hypersensitivity disease is 1 gram per cow once daily followed by 0.5 gram/cow in 2-3 days (method of administration not specified, Manning and Scheidt 1986)

10. *As palliative cataract therapy in animals which cannot go through surgery.*

Atropine's pupillary dilation property allows the animal to see *around* the axial cataract and should be administered once every three days.

11. *Treatment of uveitis.*

Atropine, a parasympathetic blocking agent, is commonly administered to the eye for treatment of uveitis. Mydriasis, the medical term for eye dilation, is one of the major effects of atropine. It does not lower the pressure in the eye.

Atropine may also be used in combination with penicillin for uveitis treatment. The antibiotic plus atropine is injected into the first layer right under the eye. It can also be used as conservative therapy when there is a rupture in the lens of the animal's eye. The laceration of the cornea is treated with topical and systemic antibiotics/corticosteroids and topical atropine. These patients are often blind and the eye is chronically inflamed if lens extraction is not performed at a latter date. (Miller, 2002a)

As a mydriatic agent, atropine keeps the eyes dilated for several days so the animal should be kept in areas where there is not a lot of sunlight because its eyes will be extremely sensitive for days after atropine administration. This is different from the effect accomplished with 0.5-1.0% tropicamide, which lasts for only a few hours.(Miller, 2002b)

Unlike other mydriatic products, atropine does not compromise the conventional aqueous outflow pathways. On the other hand, atropine has been found to improve uveoscleral outflow, which is defined as the aqueous outflow via structures other than the iridocorneal angle. The fact that the uveoscleral outflow is improved with atropine indicates that, if the animal were to have glaucoma, it would not be exacerbated, a typical side effect of mydriatic drugs on cattle suffering from glaucoma. This does not mean that atropine can be used to help *cure* glaucoma (there is definitely not enough information here to come to that conclusion), but the effects of atropine cannot make it worse.

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Atropine has also been connected with the ability to reduce the intraocular pressure in equine, but this remains controversial. Some veterinary practitioners believe that atropine can help stabilize the blood-aqueous barrier within the animal's eye while others disagree. It should be noted that most of the studies regarding this particular effect have been conducted on horses and not on cattle.(Mughannam, 1999)

The monitoring parameters used with administering atropine (dependent on dose and indication):

1. Heart rate and rhythm
2. Thirst/appetite; urination/defecation capability
3. Mouth-secretions/dryness

Parenteral atropine administration is generally performed by professional veterinarian staff and where adequate cardiac monitoring is available. If animal is receiving atropine tablets, animal must have free access to water and be encouraged to drink if dry mouth is a problem.

Historic Use by Organic Farmers: How is this material used by ORGANIC farmers?

Atropine is allowed for emergency use only because there are so few emergency options available for organic farmers. NFOA VT³ tries to provide farmers with as many emergency remedy options as possible. Atropine in general is not used extensively in organic farming due to consideration for livestock health care.(John Cleary, 2003)

Section 2119 OFPA:

Question 1: The potential of such substances for detrimental chemical interactions with other materials in organic farming systems.

There are no known interactions with other materials used in organic farming systems.

Question 2: The environmental fate of atropine and its breakdown products.

Environmental Fate:

The environmental impact of atropine use in livestock is small because of its infrequent use and its biodegradability.

The following regulatory information in the MSDS of Atropine 99%, Section 15 states the following:

Under US Federal Regulations, atropine is not included in the Health & Safety Reporting List nor is it under a chemical test rule. (CAS#51-55-8)The Clean Air Act states that the drug contains no hazardous air pollutants and Class 1 and 2 Ozone depleters. Under the Clean Water Act, none of the chemicals in atropine are listed as Hazardous Substances, Priority Pollutants and Toxic Pollutants.

At the State level, atropine is not present on state lists as an environmental hazard in CA, PA, MN, MA, FL, or NJ. Internationally, Canada does not include atropine on the Ingredient Disclosure List.(2001)

Chemical waste incineration and disposal of atropine to the municipal wastewater treatment system is done in compliance with local, state and federal regulations. The chemical structure of atropine makes this substance stable under normal

³ Northeast Organic Farming Association of Vermont

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temperatures and pressures and there has been no report of hazardous polymerization. However, exposure to direct light, dust generation, excess heat and incompatible material such as oxidizing agents should be avoided. Decomposition of large amounts of atropine can yield hazardous products such as nitrogen oxides, carbon monoxide, irritating and toxic fumes and gases, carbon dioxide and nitrogen.(2001)

The principal route of elimination is in urine, with about 30% to 50% of a dose excreted as unchanged drug. Only trace amounts can be found in the feces.⁴ Proper waste management can be used to minimize the effects of atropine in urine.

Question 3: The probability of environmental contamination during manufacture, use, misuse, or disposal of atropine.

The probability of environmental contamination depends on the source and/or the specific chemical reactions involved. The major source of atropine is the plant "*atropa belladonna*". At the end of the blooming period, the whole fresh plant without the ligneous parts of the stalk is prepared by extraction using ethanol as a solvent.(European Agency for the Evaluation of Medicinal Products Veterinary Medicines Evaluation Unit, 1998)

While 30-50% of the atropine is excreted in urine, the dose is generally small and properly handled urine should not constitute any greater contamination risk than urine from conventional farm sources.⁵

Question 4: The information provided is human adverse effects from the direct use of atropine. Human exposure is going to be through livestock. Will human exposure via livestock result in adverse consequences? What might these adverse consequences be? (see original TAP, question 5).

Atropine has a short half-life so human exposure via livestock is unlikely if healthy animals are used for meat or milk.

Atropine has been used in human medicine for over 100 years. For at least 300 to 500 years, physicians have instilled this drug on eyes. The signs of atropine poisoning are similar in all mammalian species. This includes dry mouth, thirst, difficulty swallowing, constipation, mydriasis, tachycardia, hyperpnea, restlessness, delirium, ataxia, tremulousness, convulsions, respiratory depression followed by respiratory failure which ultimately leads to death. Overdosage of the drug may cause pyrexia and tremors. (Jones & et al, 1977; Rossoff, 1974)

Human Exposure via livestock:

There is a concern that human consumption of cattle slaughtered for food while treated with atropine could lead to its effects being evident in the human consumer. The symptoms of atropinization are tachycardia, papillary dilatation, dryness of the mouth, decrease in bodily secretion, difficulty in urination and defecation.(Phone Interview, 2002a)

Atropine is rapidly absorbed from the gastrointestinal tract of an animal, with a time to peak plasma concentration of 30 minutes. Time to peak pharmacological effect is

⁴ <http://www.medsafe.govt.nz/Profs/Datasheet/l/lomotiltab.htm>

⁵ wording taken from OMRI Activated Charcoal TAP Report, August 15, 2002.

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4 to 6 hours. About 50% of a dose is bound to plasma proteins. Atropine is partially metabolized by hepatic oxidation, and distribution is throughout the body, including the CNS. Atropine has a half-life of about 4 hours.⁶ No information is available regarding meat or milk withdrawal. Atropine products are available by prescription only. Therefore, proper use and adequate withdrawal times would minimize the probability that human exposure via livestock will result in adverse health consequences.

Assuming a worst-case scenario in which a cow treated with atropine would be slaughtered and excretion of the drug has not yet occurred, a standard edible portion for meat would, in this hypothetical situation, contain far less than 1µg of the alkaloid (0.1 to 0.17µg). Also, only a trace amount of the alkaloid can be found in milk (0.05 to 0.1µg/l (20 l/day/500kg cow)).(European Agency for the Evaluation of Medicinal Products Veterinary Medicines Evaluation Unit, 1998)

Question 5: Effect of atropine use in livestock on soil organisms and crops

Atropine is a naturally occurring alkaloid of the belladonna plant. The principal route of elimination is in urine, with about 30% to 50% of a dose excreted as unchanged drug. Only trace amounts can be found in the feces.⁷ The impact on soil organisms would be through the 30-50% of the original atropine dose (generally from 0.4 mg/mL to 1.0mg/mL) in the urine. The effects of atropine (excreted in urine) on soil organisms and crops would likely be similar to the effects of the belladonna plant.

Belladonna plants are plagued by several insects, including the 'fleabeetle' and the atropine does not have any apparent adverse health effects. Rabbits, sheep, goats and swine eat the leaves with impunity, and birds often eat the seeds without any apparent effect because they synthesize atropine esterase, a potent detoxifying enzyme.⁸

Question 6: Information is needed on alternatives available in an organic system. Do not include material that cannot be used in an organic system. Do alternatives to atropine exist for dilating an animal's pupil when it has pink eye?

Alternatives for the treatment of uveitis:

1. Vaccine (For pink eye, there is a fairly new drug on the market that is actually a vaccine which can be used for prevention as well as control. It has not been approved for use in organic livestock production.)
2. Injection of cow's milk (Although not a well-known remedy in cows with pink eye, another alternative to atropine is to inject 10cc-30cc of the cow's own milk under its skin and NOT in the first layer under the eye like other medications.)(Karreman, 2002)

References

⁶ <http://www.medsafe.govt.nz/Profs/Datasheet/l/lomotiltab.htm>

⁷ Pharmacia P O Box 11-282, Ellerslie. Auckland Telephone: 09 580 4300

⁸ <http://www.botanical.com/botanical/mgmh/n/nighde05.html>

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MSDS Safety Information-Atropine, 99%. www.setonresourcecenter.com . 2001.

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ENTRIKEN, T.L. (2001) *Veterinary Pharmaceuticals and Biologicals*, 12th Edition .

Veterinary Healthcare Communications.

EUROPEAN AGENCY FOR THE EVALUATION OF MEDICINAL PRODUCTS

VETERINARY MEDICINES EVALUATION UNIT . Committee for Veterinary

Medicinal Products: Atropa Belladonna. EMEA/MRL/540/98-FINAL, 1-3. 1998.

Ref Type: Report

JOHN CLEARY, C.A.N.V. Phone interview with John Cleary, Certification

Administrator, NFOA VT. 2003.

Ref Type: Personal Communication

JONES, L.M. & ET AL (1977) *Veterinary Pharmacology and Therapeutics*. Ames: Iowa

State University Press.

KARREMAN, V.H.J. Interview with Dr. Karreman. 2002.

Ref Type: Personal Communication

MILLER, P.E. (2002a) *The Lens*.

MILLER, P.E. (2002b) *The Ophthalmologic Examination*.

MUGHANNAM, A.J.N.C.K.P.H. (1999) Effect of Topical Atropine on Intraocular Pressure and Pupil Diameter in the Normal Horse Eye. *Veterinary Ophthalmology* **2**, 213-215.

PHONE INTERVIEW, Dr. H.S. Phone Interview, Dr. Hal Sinclair, Technical Service Veterinarian, Phoenix Scientific, Inc. 2002a.

Ref Type: Personal Communication

PHONE INTERVIEW, W.I.R.C.W.a.K.C. Phone interview with Wyeth Inc.

Representative Charles Wilkins and Kelly Cashman. 2002b.

Ref Type: Personal Communication

ROSSOFF, I.S. (1974) *Handbook of Veterinary Drugs*. Springer Publishing Company, New York.