

Colchicum autumnale poisoning in a dairy farm in Switzerland: a glimpse at the milk safety aspect

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Abstract

Colchicine poisoning in livestock presents a significant challenge for dairy farming, particularly in regions where *Colchicum autumnale* (autumn crocus) is prevalent in pastures. This case report describes an incident on an organic dairy farm in Eastern Switzerland where Brown Swiss cattle showed clinical signs after consuming freshly mown meadow forage containing autumn cro-

cus leaves. The ingestion of this highly toxic plant led to severe effects such as apathy, hypothermia, and reduced milk production, which required immediate veterinary intervention. As colchicine was expected to be secreted in the milk, the milk supplier imposed a delivery stop based on European Commission Regulation (EU) No 37/2010, excluding the use of colchicine as a pharmacologically active substance in food-producing animals. Using liquid chromatography coupled to tandem mass spectrometry, it was shown that a bulk milk sample taken 2 weeks after the poisoning event tested positive, while a further bulk tank milk sample collected 5 weeks after the incident tested negative. Milk deliveries were then resumed. This paper further reviews the current understanding of colchicine as a chemical hazard in milk and presents a toxicological assessment, which is crucial for setting a detection limit for methods aimed at detecting colchicine in milk, given the absence of maximum limits and withdrawal periods following exposure. This study contributes to raising awareness of colchicine as a milk safety concern and to improving the monitoring of toxic plant exposure in livestock management (from feed to food concept).

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Case Presentation

A dairy farm in Eastern Switzerland, operating under organic farming principles, maintains a herd of 20 Brown Swiss and Pinzgauer cattle. The farm includes an ecologically valuable, species-rich meadow located on a shaded south-facing slope below a forest. This meadow supports a wide variety of plant species, including the yellow rattle (*Rhinanthus*), which is a neophyte with limited nutritional value for livestock. Due to the high presence of the *Rhinanthus* plant, the farmer obtained special permission on May 21, 2024, to cut the meadow before the usual restriction date of July 1 to prevent seed dispersal of *Rhinanthus*. The meadow was mown on May 26, 2024, and the freshly cut forage was fed directly to the dairy cows on the same day. On the evening of May 26, 2024, the cows consumed the forage as normal.

By the morning of May 27, 2024, several cows showed clinical symptoms, including apathy, loss of appetite, hypothermia, decreased milk production, and watery diarrhea. The farm veterinarian was contacted immediately, and all affected cows received symptomatic treatment with metamizole (Minalgin®), aluminum salicylate, sulfaguanidine (Inorgan®), and, in some cases, continuous infusion of acetate solution. One cow was euthanized while the remaining animals recovered over the following days.

According to the farmer, significant quantities of autumn crocus (*C. autumnale*) leaves (which were not yet in the flowering stage) were also collected during the cutting of the meadow. Typically, cows avoid consuming whole *C. autumnale* plants due to their bitter taste, but in this instance, the plants were still low-

growing and were likely ingested along with the fresh forage. The farmer's observations and clinical symptoms led to the diagnosis of a *C. autumnale* poisoning. *C. autumnale* is highly toxic due to its alkaloid colchicine. As a result, the milk supplier imposed a delivery stop of the farm milk in accordance with List 4 of the Ordinance of the Federal Department of the Interior on Maximum Residue Levels of Pharmacologically Active Substances and Feed Additives in Foods of Animal Origin (VRLtH). However, no withdrawal periods are established for milk following an accidental colchicine poisoning. In order to be able to deliver the milk, the farmer had to prove that no colchicine was detectable, in line with the self-monitoring responsibility.

At the Zurich Institute of Forensic Medicine, a quantitative analysis of colchicine was done using liquid chromatography coupled to tandem mass spectrometry: briefly, 200 μ L of milk were spiked with 50 μ L internal standard (2 ng/mL trimipramine-d3) and 50 μ L methanol. Proteins were precipitated by adding 600 μ L of acetonitrile. The samples were shaken for 10 minutes and centrifuged for 5 minutes at 10'000 rpm. 550 μ L of the supernatant was transferred into an autosampler vial, evaporated to dryness, and reconstituted in 100 μ L eluent mixture. Five external calibrator samples were prepared accordingly, replacing the methanol (MeOH) with colchicine reference standard solutions to achieve concentrations of 0.01, 0.1, 0.25, 0.5, and 2.5 ng/mL colchicine in milk. The samples were analyzed on a Nexera ultra-high performance liquid chromatography system (Shimadzu, Kyoto, Japan), coupled to a 7500 linear ion trap quadrupole mass spectrometer (Sciex, Darmstadt, Germany). The mobile phases consisted of a mixture of water (eluent A) and MeOH (eluent B), both containing 0.1% formic acid (v/v). Using a Kinetex C18 column 50 \times 2.1 mm, 2.6 μ m (Phenomenex, Aschaffenburg, Germany), the flow rate was set to 0.5 mL/min starting at 95% eluent A, decreasing to 10% within a total runtime of 20 minutes. The mass spectrometer was operated in positive electrospray ionization mode using m/z 400 \rightarrow 358 and 400 \rightarrow 310 as quantifier and qualifier ions for colchicine, respectively. To calculate the concentration of colchicine in the milk samples, a linear 1/x weighted regression model was applied to the external calibrator samples using the area ratio between the peak area of the quantifier ion and the peak area of the internal standard. Identification criteria were defined as an ion ratio of \pm 20% relative to the reference standard and a retention time tolerance of \pm 0.1 minute. The limit of detection (LOD), defined by a signal-to-noise (S/N) ratio of 3:1 for qualifier and quantifier, was estimated to be close to 0.01 ng/mL, as the S/N-ratio of the lowest calibrator (0.01 ng/mL) was approx. 9:1. As lower concentrations than 0.01 ng/mL were not relevant to the customer, the LOD was not systematically investigated. A commercially available milk sample was used as a negative control sample and did not show any interfering signals with either the quantifier or the qualifier ion.

The first bulk milk sample (17/06/24) contained colchicine at approximately 0.03 ng/mL, while in the second bulk milk sample (01/07/24), colchicine was not detected below 0.01 ng/mL, allowing milk deliveries to resume.

Colchicine as a chemical hazard

Colchicine is a tricyclic plant alkaloid contained in the autumn crocus (*C. autumnale*), which is commonly found in meadows throughout Europe (Kaltner and Hamscher, 2025). This alkaloid is

classified as a tropolone derivative and is distinguished from other typical plant alkaloids by its unique exocyclic nitrogen atom, which is located outside the core ring structure (University of Zurich, 2024). All parts of the plant are toxic, with the alkaloid concentration increasing as the plant matures. The toxic effects persist even after drying (e.g., in hay), storing, ensiling, or heating (Chizzola *et al.*, 2015; Cortinovis and Caloni, 2015; University of Zurich, 2024; Kaltner and Hamscher, 2025).

Poisonings in humans have been reported often due to confusion with the edible plant of wild garlic, *Allium ursinum* (Rao *et al.*, 2016; Giorgetti *et al.*, 2019; Wendt *et al.*, 2022). Animal poisonings have also been documented, with a lethal dose of 1 mg/kg per body weight (Chizzola and Janda, 2002; Kupper *et al.*, 2010; University of Zurich, 2024). The presence of colchicine in retail milk has not been reported; however, it is known to cross biological membranes, including the mammary gland, and it has been detected in human breast milk (Poutaraud *et al.*, 2017; Imazio *et al.*, 2020). Additionally, colchicine can transfer to the milk of grazing animals, as confirmed by studies detecting colchicine in the milk of sheep exposed to such plants (Hamscher *et al.*, 2005; Kaltner and Hamscher, 2025), highlighting the potential risk for dairy products and raising concerns regarding human exposure. Moreover, it is known that colchicine can be detected in milk for extended periods due to its slow excretion rate. Experiments with artificially contaminated milk demonstrated the persistence of colchicine also during the fermentation of milk into yoghurt (Kaltner and Hamscher, 2025). Studies on sheep suggest that colchicine concentrations in milk are comparable to those in serum, emphasizing the need for further research to assess the implications for dairy safety (Hamscher *et al.*, 2005).

Toxicological assessment

As a mitotic spindle poison, colchicine inhibits cell division during metaphase by preventing the polymerisation of tubulin, which is essential for the faithful chromosome segregation during mitotic cell division (Finkelstein *et al.*, 2010). In view of this effect, colchicine is listed in Table 2 of the European Commission Regulation (EU) No 37/2010, comprising substances for which a maximum residue limit could not be established because residues of those substances, at whatever limit, constitute a hazard to human health (European Commission, 2010). Accordingly, the use of colchicine as a pharmacologically active substance is prohibited in food-producing animals, and neither an acceptable daily intake nor a reference point for action (RPA) has been established. In Switzerland, colchicine is included in List 4, comprising banned substances (VRLtH, 2022) for which no maximum residue limits can be established.

The European Commission Regulation (EU) No. 2019/1871 could be used as a framework for managing the presence of unauthorized pharmacologically active substances in food of animal origin (European Commission, 2019). This regulation provides reference points for action in cases where such substances are detected, ensuring the safety and compliance of animal-derived food products. As a genotoxic effect of colchicine cannot be fully ruled out (Kiffe *et al.*, 2003), colchicine would need to be classified in Group I, which includes non-allowed pharmacologically active substances with direct evidence or alerts for genotoxicity, or where genotoxicity cannot be excluded. For such Group I substances, a safe limit of exposure is set at the maximum of 0.00025

µg/kg body weight per day. For a 60 kg adult drinking 1.5 liters of milk daily, this reference value amounts to:

$$\frac{0.25 \frac{\text{ng}}{\text{kg}} * 60 \text{ kg}}{1.5 \text{ l}} \text{ per day.}$$

Accordingly, protective measures should be taken if the colchicine concentration in milk reaches 10 ng/L, requiring analytical methods capable of detecting such low levels.

Beyond its presence in milk, colchicine also exhibits physiological effects on lactating animals. Specifically, it inhibits milk yield by binding to microtubules in mammary tissue, thereby interfering with cellular processes essential for lactation (Oliver and Larry Smith, 1982). The implications of this mechanism extend to both animal health and milk production efficiency in affected livestock.

Discussion

This case of colchicine poisoning in dairy cattle highlights the complex risks associated with feeding freshly mown forage from meadows that may contain toxic plants like *C. autumnale* (autumn crocus). In particular, the special permission granted to mow the meadow earlier than usual – primarily to control *Rhinanthus* populations – unintentionally increased the risk of exposure to autumn crocus leaves, as the still short leaves or seeds could not be picked out by the animals. This unfortunate sequence of events underscores the importance of a comprehensive botanical assessment before feeding freshly cut forage to livestock, especially in areas where toxic plants are prevalent.

The findings in this case are consistent with broader concerns regarding the transfer of toxins like colchicine from contaminated feed to animal tissues and milk. Previous studies have demonstrated that *C. autumnale* contamination in feed can lead to colchicine transfer into the tissues and excretions of food-producing animals, including dairy cattle (Hamscher *et al.*, 2005; Kupper *et al.*, 2010; Izzo *et al.*, 2020; Kaltner and Hamscher, 2025). This provides a natural route for the toxin to enter the food chain, potentially contaminating dairy products and posing a consumer safety issue. The presence of colchicine in milk has been documented in other animals, including sheep, and while direct evidence of colchicine in retail milk remains limited, its ability to cross biological membranes, including the mammary gland, remains a serious concern (Imazio *et al.*, 2020; Poutaraud *et al.*, 2017; Kaltner and Hamscher, 2025). Especially the persistence of the toxin after drying, storing, ensiling, or heating plays a major role in food safety, as smallest amounts can lead to adverse effects (Chizzola *et al.*, 2015; Cortinovic and Caloni, 2015; University of Zurich, 2024; Kaltner and Hamscher, 2025).

The legal framework regulating the presence of colchicine in animal-derived foodstuffs – such as its inclusion into the list of pharmacological substances – demonstrates the importance of strict monitoring. Although there are no set withdrawal periods for milk after colchicine poisoning, this case shows that it is possible to detect traces of the toxin using modern analytical methods. The negative test result of the second bulk milk sample allowed the resumption of milk deliveries and underlined the crucial role of regular monitoring in ensuring the safety of dairy products.

The risk management approach should focus on prevention, emphasizing the need for improved pasture and forage manage-

ment strategies (from the feed to food concept). In particular, farmers should be encouraged to regularly check the botanical composition of their pastures and ensure that no toxic plants are present in the feed for livestock, especially when cutting and feeding freshly mown forage from extensively used pastures.

Conclusions

This case report of a colchicine poisoning in dairy cattle illustrates the risks associated with the ingestion of *C. autumnale* and the potential contamination of milk with colchicine. The unintentional exposure of the herd to colchicine due to the early mowing of a meadow containing autumn crocus leaves serves as a reminder of the importance of vigilance in pasture management. While the regulatory framework and analytical methods provide procedures to ensure the safety of dairy products, it is the responsibility of farmers to minimize exposure to toxic plants. By improving pasture and feed management practices and adopting regular testing for plant toxins, the likelihood of such incidents can be reduced in the future. In the broader context, these measures will contribute to the protection of public health by minimizing the potential for toxin transfer into the food chain. Moreover, the potential use of the described methodology, and particularly the relevance of the 10 ng/L value as an RPA, could be further discussed within European Union reference laboratories. Future studies should include milk sampling directly from the udders of deceased animals to better establish correlations with lethal doses and the corresponding milk levels.

References

- Chizzola R, Bassler-Binder G, Winter S, Zebeli Q, Kriechbaum M, 2015. Persistence of alkaloids of typical poisonous plants autumn crocus and marsh ragwort in grass silage. *Wiener Tierärztliche Monatsschrift* 102:285-92.
- Chizzola R, Janda P, 2002. Intoxication of sheep by autumn crocus in the hay. *Wiener Tierärztliche Monatsschrift* 89:4-7.
- Cortinovic C, Caloni F, 2015. Alkaloid-containing plants poisonous to cattle and horses in Europe. *Toxins* 7:5301-7.
- European Commission, 2010. European Commission Regulation (EU) No. 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin. In: *Official Journal*, L 15/1, 20/01/2010.
- European Commission, 2019. European Commission Regulation (EU) No. 2019/1871 of 7 November 2019 on reference points for action for non-authorized pharmacologically active substances in foodstuffs of animal origin and repealing Decisions 2005/34/EC. In: *Official Journal*, L 290/1, 07/11/2019.
- Finkelstein Y, Aks SE, Huston JR, Juurlink DN, Nguyen P, Dubnov-Raz G, Pollak U, Koren G, Yedidia B, 2010. Colchicine poisoning: the dark side of an ancient drug. *Clin Toxicol* 48:407-14.
- Giorgetti A, Nalesso A, Cecchetto G, Pizzi M, Bellan A, Viel G, Montisci M, 2019. Two fatal intoxications by colchicine taken for saffron. *Clinical, medico-legal and forensic toxicological implications*. *Leg Med* 38:64-8.
- Hamscher G, Priess B, Nau H, Panariti E, 2005. Determination of colchicine residues in sheep serum and milk using high-performance liquid chromatography combined with electrospray ion-

- ization ion trap tandem mass spectrometry. *Anal Chem* 77:2421-5.
- Imazio M, Andreis A, Brucato A, Adler Y, De Ferrari GM, 2020. Colchicine for acute and chronic coronary syndromes. *Heart* 106:1555-60.
- Izzo L, Rodríguez-Carrasco Y, Tolosa J, Graziani G, Gaspari A, Ritieni A, 2020. Target analysis and retrospective screening of mycotoxins and pharmacologically active substances in milk using an ultra-high-performance liquid chromatography/high-resolution mass spectrometry approach. *J Dairy Sci* 103:1250-60.
- Kaltner F, Hamscher G, 2025. Colchicine as a food contaminant: rare occurrence but persistent in stored honey and during yogurt fermentation. *J Consum Prot Food Saf* <https://doi.org/10.1007/s00003-025-01541-z>.
- Kiffe M, Christen P, Arni P, 2003. Characterization of cytotoxic and genotoxic effects of different compounds in CHO K5 cells with the comet assay (single-cell gel electrophoresis assay). *Mutat Res* 537:151-68.
- Kupper J, Rentsch K, Mittelholzer A, Artho R, Meyer S, Kupferschmidt H, Naegeli H, 2010. A fatal case of autumn crocus (*Colchicum autumnale*) poisoning in a heifer: confirmation by mass-spectrometric colchicine detection. *J Vet Diagn Invest* 22:119-22.
- Oliver SP, Larry Smith K, 1982. Milk yield and secretion composition following intramammary infusion of colchicine. *J Dairy Sci* 65:204-10.
- Poutaraud A, Michelot-Antalik A, Plantureux S, 2017. Grasslands: a source of secondary metabolites for livestock health. *J Agric Food Chem* 65:6535-53.
- Rao R, Seshadri S, Patil N, Rao K, Nayak V, Dsouza H, Jaunky C, 2016. Fatal poisoning with colchicum autumnale: a case report. *RJPBCS* 7:1760-2.
- University of Zurich, 2024. CliniTox Pflanzengifte: Colchicum autumnale. Available from: https://www.vetpharm.uzh.ch/gift-db/pflanzen/0022_tox.htm. Accessed on: 28/02/2025.
- VRLtH, 2022. SR 817.022.13. Available from: https://www.fedlex.admin.ch/eli/cc/2017/154/de_ [Material in German].
- Wendt S, Prasa D, Lübbert C, Begemann K, Franke H, 2022. Food poisoning from fruits in Germany. *Dtsch Arztebl Int* 119:333-4.