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# Aversion Properties of Retrorsine, Retrorsine Nitrogen Oxide and Frosted Senecio latifolius


## Abstract

Two pilot trials, investigating the aversive properties of retrorsine and retrorsine nitrogen oxide and that of frosted *Senecio latifolius*, were executed. Retrorsine and retrorsine-NO (the toxic principles of *Senecio retrorsus*), unlke sceleratine-NO (the toxic principle of another hepatotoxic pyrrolizidine alkaloid containing plant, namely *S. latifolius*), were not capable of establishing aversion when given to a sheep. Frosted *S. latifolius* given to a sheep also did not induce aversion. However, a sheep averted to *S. latifolius* (non-frosted) refused eating frosted *S. latifolius*.



## Keywords

aversion properties, retrorsine, retrorsine-NO, frosted S. latifolius



## Cover Page Footnote

Footnote LD Snyman: Retired veterinary research scientist (snymanleendert@gmail.com)



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*Senecio* species such as *Senecio latifolius* and *Senecio retrorsus* cause significant economic losses in South Africa when grazed by livestock due to the hepatotoxic pyrrolizidine alkaloids they contain (Kellerman *et al*. 1996). It was previously reported (Snyman 2023) that sceleratine nitrogen oxide (sceleratine-NO), the toxic principle of *S. latifolius*, has aversive properties and thus could potentially be used for establishing aversion in livestock to prevent *S. latifolius* poisoning. The question arises whether the aversive characteristics of sceleratine-NO are representative of hepatotoxic pyrrolizidine alkaloids in general? Two pilot studies were conducted to determine if retrorsine and retrorsine-NO, the hepatotoxic pyrrolizidine alkaloids found in *S. retrorsus* (Kellerman *et al*. 2005) would be aversive when administered in sheep, similar to sceleratine-NO. An additional pilot study was conducted to determine if *S. latifolius*, when frosted during a very cold winter night, would retain it's aversive properties. As these characteristics may be of practical significance.

**Aversion properties of retrorsine and retrorsine-NO**. All animal procedures in this study were carried out according to the South African National Standard (The Care and Use of Animals for Scientific Purposes [SANS 10386:200X]. All animal experiments were approved by the ARC-OVI Animal Ethics Committee.

Two naïve Dorper sheep (approximately 50 kg) individually housed in pens (1 x 3.5 metre) were each offered 6 mg retrorsine mixed with 100 g maize meal according to the procedure described for sceleratine-NO (Snyman 2023). After complete consumption of the mixture Sheep 1 and Sheep 2 were orally drenched (using a drench gun) with 35 mg and 81 mg retrorsine (mixed with 100 ml propylene glycol), respectively. Both sheep consumed all of the retrorsine containing meal mixture when offered again 24 h. later (Fig. 1). Thus no aversion to retrorsine was established in either sheep, despite the fact that Sheep 2 ingested twice the amount required to previously avert sheep with sceleratine-NO (Snyman 2023). Serum aspartate aminotransferase (AST) and gamma glutamyl transferase (GGT) activities (Units/L) of 94 and 55, respectively, for Sheep 2, 48 h. after treatment, tended to be higher than the normal reference range, an indication of possible hepatic damage. Values for Sheep 1 were found to be in the normal range.

In a second pilot study aversion to retrorsine-NO was investigated. Two Dorper sheep (approximately 50 kg and housed as described above), namely Sheep 3 and Sheep 4, were drenched similar to retrosine but with 39 mg and 85 mg retrorsine-NO, respectively, after total consumption of a sceleratine-NO containing maize meal mixture (7 mg/100 g maize meal). Both sheep completely consumed the sceleratine-NO containing meal mixture again when presented on Day 2 (Fig. 2). Retrorsine-NO also revealed no aversive property, similar to results with retrosine.

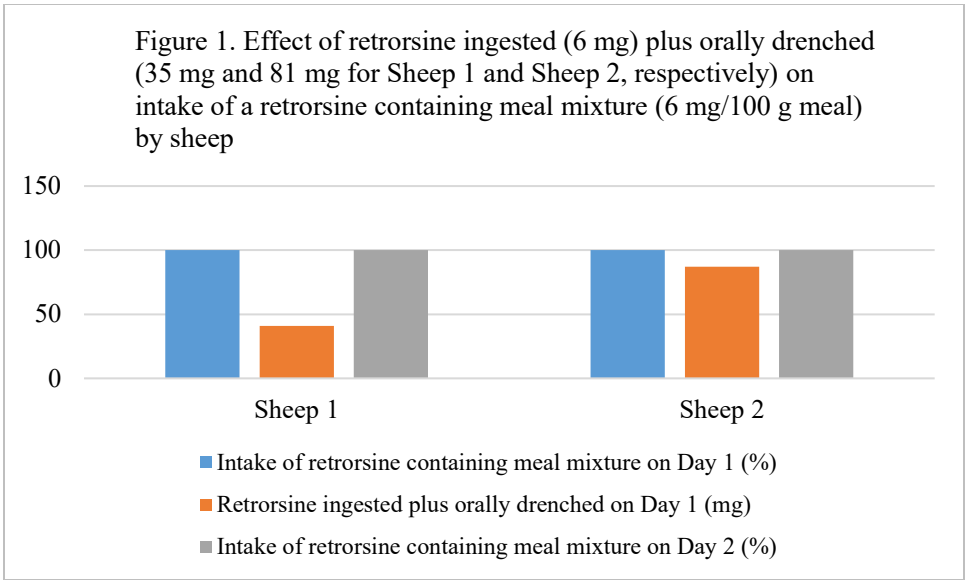



Figure 1. Effect of retrorsine ingested (6 mg) plus orally drenched (35 mg and 81 mg for Sheep 1 and Sheep 2, respectively) on intake of a retrorsine containing meal mixture (6 mg/100 g meal) by sheep

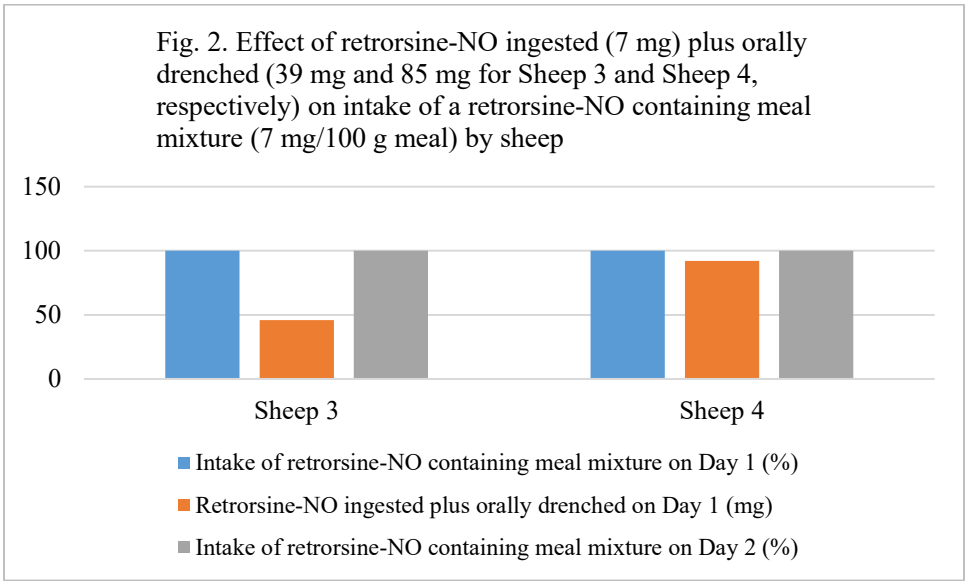


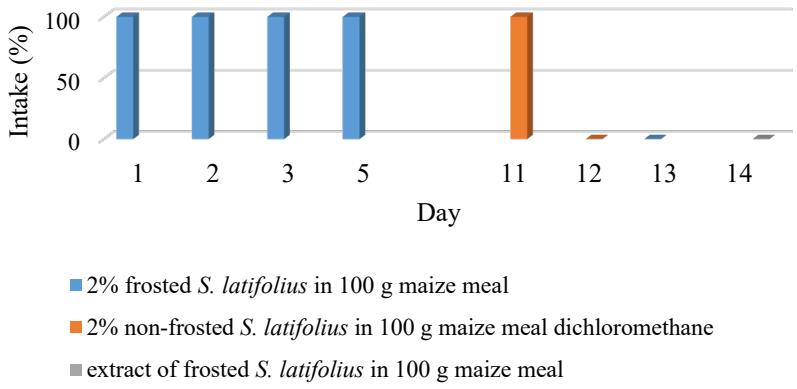

Fig. 2. Effect of retrorsine-NO ingested (7 mg) plus orally drenched (39 mg and 85 mg for Sheep 3 and Sheep 4, respectively) on intake of a retrorsine-NO containing meal mixture (7 mg/100 g meal) by sheep

The results from these two pilot studies are similar to those of a previous study with digitoxin (Kellerman *et al*. 1991 – 1994) in that sheep that received increasing doses, ranging from 5 to 80 mg, could not be averted despite clinical signs of mild cardiac glycoside poisoning. These results are contrary to the effect of another cardiac glycoside namely epoxyscillirosidin which established aversion in steers with doses as low as 0.06 mg/kg BW (9.6 mg/160 kg steer) (Snyman *et al*. 2004). These preliminary results suggest that the aversion inducing capability of a

toxin might not necessarily be related to the chemical grouping to which it belongs. If proven, these observations might be of theoretical and practical significance.

**Aversion properties of frosted S. latifolius.** *Senecio latifolius* that became frosted the previous night was collected early in the morning, freeze dried with a Christ laboratory freeze drier and milled with a Wiley cutting mill through a 1 mm sieve. A naïve Dorper wether (approximately 50 kg), individually housed in a pen (1 x 3.5 metre), was offered 100 g of 2% frosted *S. latifolius* in maize meal on Day 1. After total consumption of the mixture the sheep was dosed *via* a stomach tube with an additional 18 g of frosted *S. latifolius* shaken up in water. The 2% frosted *S. latifolius* in maize meal was totally consumed when presented on Days 2, 3, and 5 again. On Day 11 the sheep was offered 100 g of 2% non-frosted (freeze dried and milled) *S. latifolius* in maize meal. The mixture was totally consumed. This was followed by dosing 18 g of the non-frosted *S. latifolius via* a stomach tube directly thereafter. The sheep was then challenged with 2% non-frosted *S. latifolius* in 100 g maize meal on Day 12, 2% frosted *S. latifolius* in 100 g maize meal on Day 13, and a dichloromethane extract (prepared as formerly described by Snyman 2023) of frosted *S. latifolius* in 100 g maize meal (equivalent to 2% frosted *S. latifolius*) on Day 14. All three of the presentations were totally refused. The results are shown in Figure 3.

Figure 3. Intake of frosted and non-frosted *S. latifolius* and a dichloromethane extract of frosted *S. latifolius* by a sheep after treatment for aversion to frosted and non-frosted *S. latifolius* on days 1 and 11, respectively




Total intake of frosted *S. latifolius* after dosage with 18 g of the plant material indicates no aversive effect in contrast with non-frosted *S. latifolius*, which was totally refused after the sheep was dosed with the same amount of plant material, suggesting disappearance of the aversive property during frosting. This might also suggest a loss in toxicity as well (Riley and Tuck 1985). Total refusal of

frosted *S. latifolius* on Day 13 and of a dichloromethane extract of the frosted *S. latifolius* on Day 14 after aversion was established to non-frosted *S. latifolius*, however, indicates retention of the sensory characteristics during frosting.

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