Management of three toxic Delphinium species based on alkaloid concentrations

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Received 4 January 2001; accepted 1 May 2001

Abstract

A systematic approach to the taxonomic classification of the tall larkspur complex (Delphinium spp.) has been developed and implemented using molecular genetics, plant morphology, and alkaloid profiles, as shown in other papers in this series. This approach supports the classification of three distinct species (D. glaucum, D. barbeyi and D. occidentale), as the species differ in genetics and toxicity. Toxic alkaloid concentrations over the growing season were integrated with data on diet selection to make management recommendations on a species-specific basis to reduce the risk of poisoning cattle. Alkaloid concentrations in tall larkspurs in excess of 3 mg/g impart moderate or high risk to grazing cattle if sufficient quantities are consumed. D. glaucum is most toxic, with toxic alkaloid concentrations that exceed 3 mg/g throughout the grazing season until late maturity. Cattle should be denied access to dense patches of this species throughout the grazing season until after seed shatter. Concentration of toxic alkaloids in D. barbeyi is highest in vegetative plants, but D. barbeyi is unpalatable to cattle until flowering racemes begin to elongate. We recommend grazing D. barbeyi ranges early in the season when it is not palatable, then removing cattle from early flowering stage through mid-pod stage when cattle are most likely to be poisoned. Cattle can again safely graze D. barbeyi late in the season when the toxic alkaloid concentration typically declines below 3 mg/g. Some populations of D. occidentale and the D. barbeyi×D. occidentale hybrids do not contain toxic alkaloids, and pose little risk of poisoning throughout the year. Toxicity of northern populations of D. occidentale varies from year-to-year for unknown reasons. Cattle
losses from *D. occidentale* are usually less severe than from *D. barbeyi*, but generally the same recommendations apply as for *D. barbeyi*. Toxicity sampling is an essential management tool. Tall larkspur populations can be tested for toxicity throughout the growing season. Whenever toxic alkaloid concentrations exceed 3 mg/g in leaves, flowers, or pods, cattle should be removed from the area and not returned until pods begin to shatter and risk of poisoning is lower. In general, tall larkspurs are safe to graze when alkaloid concentrations fall below 3 mg/g because it is difficult for cattle to eat sufficient larkspur to become fatally poisoned.

Published by Elsevier Science Ltd.

**Keywords:** Delphinium glaucum; Delphinium barbeyi; Delphinium occidentale; Diterpenoid alkaloids; Methyllycaconitine; Larkspurs; Poisonous plants; Cattle grazing

1. **Introduction**

Tall larkspurs *Delphinium* spp. are recognized throughout the western US as a significant poisoning threat to cattle on mountain rangelands (Pfister et al., 1999). Because of their distinctive spur-shaped flower, tall robust stature, and similar habitats where they grow, the four major species are all locally referred to as “tall larkspur”. Nonetheless, larkspur species differ substantially in toxicity (Ralphs et al., 1997; Gardner et al., 2002). The common nomenclature makes it difficult to communicate unambiguous information about potential toxicity and to integrate toxicity into management scenarios to reduce risk to grazing cattle.

Furthermore, there is disagreement in the formal taxonomic classification of the tall larkspur complex. Ewan (1945) originally classified three species of tall larkspur (*D. glaucum*, *D. barbeyi*, and *D. occidentale*) based on pubescence in the inflorescence, flower size and shape, leaf structure, and geographical distribution. Two species (*D. barbeyi* and *D. occidentale*) hybridize where the populations merge in central Utah, leading Welsh (1987) to classify *D. barbeyi* as a variety of *D. occidentale*. Recently, Warnock (1995) regrouped the tall larkspur complex, as he assigned all of Ewan’s *D. occidentale* to *D. glaucum*, restricted *D. barbeyi* to a small area on the top of the Wasatch Plateau in central Utah, and referred to the remainder of *D. barbeyi* as a hybrid with *D. glaucum* under the name of *D. occidentale*. A clear, concise grouping of tall larkspurs, based on chemical profiles (Gardner et al., 2002), alkaloid structure and toxicity (Panter et al., 2002), genetics (Li et al., 2002) and morphology (Welsh and Ralphs, 2002) is necessary for this economically-important group of plants to convey accurate and reliable information to natural resource managers and livestock producers. Once larkspur species are clearly defined, management recommendations can be tailored for individual species to reduce the risk of poisoning.

2. **Concurrent research**

Gardner et al. (2002) analyzed the chemical profile and concentrations of individual norditerpene alkaloids from 18 larkspur populations covering a wide geographical
area in the western US. The chemical profile of Ewan’s *D. glaucum* was shown to be distinct from the other entities, with two alkaloids unique to *D. glaucum*. Concentration of the dominant toxic alkaloid, methyllycaconitine (MLA), was highest in *D. glaucum*. Clusters of Ewan’s *D. barbeyi* and *D. occidentale* were also distinct. Although several alkaloids were common to *D. barbeyi* and *D. occidentale*, the two species differed in toxic alkaloid concentration. Warnock’s (1995) broad classification of *D. glaucum* and splintering of *D. barbeyi* was shown to be inappropriate (Li et al., 2002; Gardner et al., 2002; Welsh and Ralphs, 2002).

Li et al. (2002) assessed the genetic diversity of tall larkspurs using DNA markers. They found that the three species conformed closely to Ewan’s classification. *D. glaucum* was genetically distant from *D. occidentale*, whereas *D. barbeyi* and *D. occidentale* hybrids had markers of both parental groups. Additionally, Welsh and Ralphs (2002) compared the previous taxonomic classification schemes (Ewan, 1945; Hitchcock and Cronquist, 1973; Welsh, 1987; Warnock, 1995). The work of Welsh and Ralphs (2002) resulted in a revised dichotomous key using morphological and geographical criteria and also indicated that *D. occidentale*, *D. glaucum* and *D. barbeyi* are separate species.

Over 40 norditerpenoid alkaloids are found in tall larkspur species. Panter et al. (2002) tested the toxicity of the 16 major alkaloids using i.v. injections into mice. The methylsuccimidoanthronyllycoctonine (MSAL) group of alkaloids is most toxic (Manners et al., 1995). As noted above, the MSAL alkaloid MLA dominates this group. The lycoctonine group of alkaloids is intermediate in toxicity, whereas the MSAL alkaloids are an order of magnitude more toxic than the methylenedioxy (MDL) alkaloids. The MDL alkaloid deltaline typically occurs at higher concentrations than any other alkaloid found in larkspurs (Manners et al., 1995; Panter et al., 2002).

3. Mechanism of action and toxicity

The mechanism of action of the toxic class of alkaloids is neuromuscular paralysis. Nicotinic acetylcholine receptors in the muscle and brain are blocked by MLA (Aiyar et al., 1979; Dobelis et al., 1999) causing muscular fatigue and depressed respiration. Clinical signs of intoxication in cattle include muscular weakness and trembling, straddled stance, periodic collapse into sternal recumbency, and finally death from respiratory failure while in lateral recumbency. Bloat may occur and contribute to death, due to reduction in rumen motility and paralysis of the eructation mechanism. Death may be prevented if intoxicated animals are given cholinergic drugs such as phystostigmine (Pfister et al., 1994a), but administering drugs under extensive range-land situations is problematic.

The effective dose of MLA that causes muscular tremors and periodic collapse in cattle is 21 mg/kg BW (Pfister et al., 1994b; 1997a). The lethal single dose was estimated at 40 mg/kg BW through a series of extrapolations (Pfister et al., 1999), and repeated daily doses are undoubtedly fatal at lesser, but unknown, amounts.

Larkspur alkaloid concentrations have been determined for individual alkaloids
(Gardner et al., 1999) and for total toxic alkaloids (Gardner et al., 1997). The assay for total toxic alkaloids provides the total concentration of MLA and all other MSAL-type alkaloids in the plant material. The management recommendations we provide in this paper are based on concentrations of total toxic (MSAL-type) alkaloids in tall larkspurs.

Alkaloid concentrations are highest in the new early growth of all three species. Concentration of toxic alkaloids in *D. barbeyi* was 25 mg/g during early growth in late June (Ralphs et al., 2000) and declined as the plants matured to levels below 1 mg/g as the plants senesced in September (Gardner and Pfister, 2000). In early July when cattle generally enter larkspur areas (bud stage), concentration of MSAL alkaloids dropped to 8 mg/g. A mature cow consumes about 12 kg/day of forage on a dry matter (DM) basis. Thus, a cow would have to eat about 1.13 kg (DM) of larkspur to cause collapse. Later in August when larkspur matures to the pod stage and concentration of MLA drops to 3 mg/g, an intoxicating dose would be about 3 kg DM of larkspur (=15 kg fresh weight), or greater than 25% of the daily diet. The risk of poisoning based on toxic alkaloid concentration has been classified as: low toxicity (<3 mg/g); moderate toxicity (3–6 mg/g); and highly toxic (>6 mg/g) (Pfister et al., 1997a).

### 4. Plant/animal interactions

The risk of poisoning is determined by both the concentration of toxic alkaloids in the plant and the acceptability of larkspur to cattle. Toxicity of larkspur declines as it matures, but palatability increases. Pfister et al. (1988) proposed a toxic window based on these observations (Fig. 1). From a series of nine grazing studies, Pfister et al. (1997a) reported that cattle did not eat *D. barbeyi* or *D. occidentale* in their early growth stages. Consumption began as the plants began to elongate flowering racemes, and increased as larkspur matured into the pod stage. As the plants advance into the mature pod stage, however, the alkaloid concentration is often sufficiently low that a cow cannot eat larkspur rapidly enough to ingest a fatal dose. Thus, the 4–5 week period from bud elongation to mature pods is the critical period when many animals are poisoned. Pfister et al. (1997b) developed a quantitative model based on toxic alkaloid concentration and consumption of larkspur as a percentage of daily diet to predict the risk of poisoning (Fig. 2). This model has been used to develop a decision-making flow chart to guide management decisions about when to graze tall larkspur and when to deny access to the plants (Pfister, 1999).

Previous studies showed no relationship between concentration of total and toxic alkaloids and larkspur palatability to cattle (Pfister et al., 1996). Thus, higher alkaloid concentrations alone appear to be unimportant in altering flavor and reducing short-term (i.e., within meal) consumption by cattle. Although single-meal larkspur consumption by cattle is not negatively influenced by high alkaloid concentrations, sublethal intoxication and multi-day consumption patterns are partially dependent on toxic alkaloid concentrations. Larkspur ingestion by cattle above a toxic threshold is regulated by postingestive consequences in a dose-dependent manner (Pfister et
Fig. 1. Relative relationship between tall larkspur toxicity and palatability. *Delphinium* spp. (tall larkspur) toxicity declines as the plants mature, however, palatability to cattle usually increases once flowering occurs. Cattle generally do not prefer tall larkspur until flowering racemes have elongated; thus, the primary toxic window for potentially fatal intake occurs between the flowering and the early pod stage of growth.

al., 1990). Cattle limit ingestion of larkspur (i.e., dose of toxic alkaloids) so that periods of high consumption (1 to 2 days) are followed by periods of reduced consumption (1 to 3 days). This cyclic consumption pattern apparently allows for detoxification after episodes of intoxication (Pfister et al., 1997b). Cattle apparently increase consumption because larkspur is very nutritious (e.g., 15–20% crude protein; Pfister et al., 1988), but then decrease consumption due to toxic feedback in a dose-dependent fashion. Cyclic consumption generally enables cattle to regulate larkspur consumption below a subclinical toxic threshold (14 to 18 mg toxic alkaloid/kg), and allows cattle to periodically graze this toxic but nutritious plant. On larkspur-infested rangelands during periods when cattle are eating tall larkspur, we have documented that every animal observed will eat some larkspur, yet only some (5 to 15%) are fatally poisoned in a grazing season. Our observations indicate that many cattle deaths occur after brief (30 to 90 min) periods of over ingestion during summer storms (Pfister et al., 1988; Ralphs et al., 1994), and death likely occurs before negative postingestive feedback works to temporarily reduce larkspur consumption.

5. Ecology and management recommendations

Published accounts of toxic alkaloid concentrations over the growing season (Pfister et al., 1994c; Ralphs et al., 1997) and during senescence (Gardner and Pfister, 2000), along with observations on diet selection by cattle (Pfister et al., 1997a),
Fig. 2. Anticipated risk of death loss (high, moderate, low) in cattle when consuming *Delphinium* spp. (tall larkspur) based on its toxic alkaloid concentration (mg/g) and the percent (%) of larkspur in the diet. Death losses are generally low or non-existent before flowering because consumption of larkspur by cattle is low or nil; after larkspurs begin to flower risk can vary from low to high depending on amount eaten and toxicity of the plant material.

have been integrated to make specific management recommendations for each of the three species.

5.1. *D. glaucum*

*D. glaucum* occurs along stream banks, in willow thickets, and along edges of wet subalpine meadows as a minor component of the plant community (Looman, 1984). It is a tall (1–2.5 m), robust plant (up to 30 stalks/plant). *D. glaucum* generally grows as isolated plants, but occasionally grows in dense patches in the San Gabriel, Klamath and Sierra Nevada mountains in California, and the Cascade and Olympic mountains in Oregon and Washington.

*D. glaucum* is the most toxic of the tall larkspurs in the US, containing the highest levels of the toxic alkaloids MLA and 14-deacetylnudicauline (DAN; Gardner et al., 2002). In our studies, mean concentration of MLA in *D. glaucum* from California was 19.5 mg/g, compared to 9 mg/g in *D. barbeyi*, and 3.5 mg/g in *D. occidentale* over the summer growing season. Exclusive of the two southern most collections of *D. barbeyi* (Cedar City and Salina, UT), there was no overlap in confidence intervals for toxic alkaloid concentrations for the other two species and *D. glaucum* collected before the pod stage. Even though toxic alkaloid concentration declined through the
growing season, toxic alkaloid concentrations in *D. glaucum* remained above 3 mg/g until after seed shatter (Ralphs et al., 1997), and ripe pods contained 4.9 mg/g (Gardner and Pfister, 2000). Therefore, *D. glaucum* appears to remain highly toxic throughout most of the grazing season.

No grazing studies have been conducted with *D. glaucum* to determine when it is preferred by cattle. Nonetheless, historical losses of cattle have been large where it grows in thick patches (Marsh and Clawson, 1916). Furthermore, heavy winter snow in the Sierra Mountains may retard summer flowering in *D. glaucum* until late summer, thus extending the toxic window to late August and September (Chesnut and Wilcox, 1901). After pods ripen and shatter, toxic alkaloid concentrations decrease rapidly and risk to cattle is low (Gardner and Pfister, 2000). Our recommendation is to restrict cattle access to this species throughout the growing season until seed shatter which typically occurs in late August or September.

### 5.2. *D. barbeyi*

*D. barbeyi* occurs in the southern Rocky Mountains from southcentral Wyoming through Colorado into northern New Mexico, and from central Utah southward. Ellison (1954) found that it was a principal component of the mixed upland herb association, comprising 2–5% of total cover, ranging up to 50% in some areas. Tall larkspur is also one of the most conspicuous species of the tall forb community in snow drift sites and at the edge of wet meadows and along streams along the top of the Wasatch Plateau in central Utah. The plant is also a dominant component of the tall forb plant community growing beneath aspen throughout its distribution. It thrives in areas where soil moisture is not limiting (snow drift sites, and in the region of summer monsoonal thunderstorms). *D. barbeyi* is a tall (1–2 m), robust plant (20–150 stalks/plant), and tenaciously long-lived (>75 years; Cronin and Nielsen, 1979).

During the grazing season, the concentration of toxic alkaloids in *D. barbeyi* declined from 12 to 2 mg/g (Ralphs et al., 1997). Alkaloid concentrations in pods and leaves late in the season fell below 3 mg/g (Gardner and Pfister, 2000). The extensive history of grazing studies on *D. barbeyi* indicates that cattle will not graze it until flowering begins (Pfister et al., 1997a,c). Thus, we recommend stocking during the early/late season as proposed by Pfister et al. (1997a) to avoid the high risk of poisoning during the toxic window from bud elongation to mature pod stage. Cattle can graze in larkspur-infested areas early in the season before flowering begins; this allows utilization of the other nutritious forage that grows in association with larkspur. Cattle should be removed from larkspur-infested areas during the flowering period when it is most palatable, but can be returned to these areas as pods mature and toxicity drops below dangerous levels.

### 5.3. *D. occidentale*

*D. occidentale* occurs in the northern Rocky mountains from northern Utah into western Wyoming, Idaho, Montana, and throughout the basin and range mountains of Nevada. It grows mostly under aspen and in more mesic areas in depressions of
the mountain big sagebrush plant community. It also grows from 1–2 m, but is not as robust as *D. barbeyi*, with generally fewer than 10 stalks/plant. *D. occidentale* grows in areas where summer drought is common, thus it typically matures and senesces by mid to late summer.

Populations of *D. occidentale* in northern Utah (e.g., near Logan) contain little or no MLA. Further, *D. barbeyi × D. occidentale* hybridize where populations overlap, thus extending the range southward in Utah and into Colorado. These hybrid populations also contain little or no MLA and would provide safe and nutritious forage at any time. Variation in MLA concentration is substantial between the northern US populations and among years (Ralphs et al., 1997). Some locations (e.g., Bozeman, Montana and Jackson, Wyoming) and years remained below 3 mg/g throughout the grazing season, and thus would pose little risk of poisoning. MLA concentrations in populations of *D. occidentale* in southern Idaho generally remain above 4 mg/g until the pods mature and shatter (Ralphs et al., 1997; Gardner and Pfister, 2000), thus posing a moderate risk (Fig. 2) until late in the grazing season.

A rapid test for larkspur toxic alkaloids is available at the USDA/ARS Poisonous Plant Research Laboratory. Samples from questionable populations may be analyzed early in the season to determine relative risk. If concentration of toxic alkaloids exceeds 3 mg/g during the flowering stage, cattle may be removed during this toxic window, then returned after pods have matured.

6. Conclusions

Concentration of the toxic alkaloid MLA generally accounts for the difference in toxicity among the tall larkspur species. Sampling of tall larkspurs to determine MLA and total toxic alkaloid concentrations has been integrated with data on selection of larkspur by grazing cattle to determine relative risk of poisoning. We determined that *D. glaucum* was most toxic, with toxic alkaloid concentration exceeding 3 mg/g until late maturity. The management recommendation is to restrict cattle access to dense patches of this species until pods shatter. The toxic alkaloid concentration of *D. barbeyi* typically declines well below 3 mg/g during the pod stage. Therefore, we recommend grazing early in the season when it is not palatable, removing cattle during the toxic window from bud elongation (early flowering) through mid pod stage, then allowing grazing late in the season. Some populations of *D. occidentale* and the *D. barbeyi × D. occidentale* hybrid do not contain MLA, and are not toxic. Toxicities of northern US *D. occidentale* populations vary among years for unknown reasons. A rapid and accurate assay is now available to measure toxic larkspur alkaloids in plant samples. Populations should be tested during the flowering and pod stages of growth. If toxic alkaloid concentration exceeds 3 mg/g during the flowering stage when cattle often initiate consumption, cattle should be removed until pods shatter in August or September. If the toxic alkaloid concentration in pods exceeds 3 mg/g, risk will at least be moderate if cattle are eating pods. Larkspur with lower concentrations of toxic alkaloids in leaves, flowers, and pods should be safe to graze throughout the growing season as it is difficult for cattle to eat sufficient quantities to be fatally poisoned.
Acknowledgements

We thank Kermit Price, Derek Hinkley, and Lee Woolsey for their excellent technical assistance in various tall larkspur studies. We also thank Dr Dean Anderson and Dr Bret Olson for helpful review comments.

References


