

Behavioral Strategies for Coping with Poisonous Plants

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Abstract

Poisonous plants are an integral component of most rangelands in the western U.S. Although domestic livestock losses can be severe, obviously most wild and domestic animals grazing on rangelands do not die of toxic plant ingestion. Grazing animals use several interrelated behavioral and physiological strategies to reduce the risk of poisoning: (1) avoid or reduce toxin intake through changes in diet selection; (2) select a mixed diet and dilute the toxin; (3) consume a toxin in a cyclic or intermittent fashion; (4) eject a toxin once eaten; (5) complex, degrade, detoxify, and (6) tolerate the toxin once eaten. A central tenet of the first 3 strategies includes postingestive consequences and aversive conditioning, whereby animals learn from the negative or positive consequences of eating particular forages. The last 3 strategies describe how animals handle toxins once consumed. When livestock reject toxic plants in favor of less toxic or nontoxic species, learning is usually involved. Domestic livestock losses attest that learning is not a perfect avoidance mechanism. Nonetheless, learning enables most livestock to survive grazing on ranges with poisonous plants. Domestic livestock are more often harmed by toxic plants than are wild ungulates, probably because many livestock losses result from human management errors that override coping strategies. Furthermore, wildlife survival is probably enhanced by increased capacity to tolerate or detoxify toxins relative to livestock.

Introduction

Poisonous plants have long been a topic for legends and scientific inquiry. The toxin is the plant compound responsible for the plant's effects, and the word is derived from the Greek word *toxikon*, or 'poison for arrows'. This paper is concerned, not with poisonous projectiles,

but with plants poisonous to grazing animals. In the western United States, poisonous plants are ubiquitous on many rangelands, but domestic or wild ungulates grazing on rangelands do not usually succumb to poisonous plants. Although most survive, some obviously don't. Indeed, losses of domestic livestock to poisonous plants exceed \$300 million per year (Nielsen et al. 1988), not including goats and horses. No figures are available for wildlife, but losses do occur (Fowler 1983). Economic impacts of toxic plants range from death and abortion to lost grazing opportunities (Table 1). Good range condition helps to reduce losses to some poisonous plants. Nevertheless, poisonous plants also kill or impair grazing animals on good condition rangelands because these plants are integral components of many rangeland communities, and at times are acceptable forages (e.g., larkspur, chokecherry, veratrum, water hemlock, oakbrush, pine needles, halogeton, greasewood). A partial list of important toxic plants is given in Table 2.

Grazing animals use several behavioral and physiological strategies or adaptations to reduce the risk of poisoning. There are at least 6 strategies by which animals can avoid or reduce toxicity from plants: (1) avoid or reduce toxin intake through changes in diet selection; (2) select a mixed diet to dilute the effect of specific toxins; (3) consume a toxin in a cyclic or intermittent fashion to avoid permanent injury; (4) eject a toxin once eaten; (5) complex, degrade, or detoxify the toxin; and (6) tolerate the toxin once eaten. These categories are not mutually exclusive as there is substantial overlap. In general the first 3 strategies involve reducing or eliminating consumption of a toxin through behavioral changes, whereas the last 3 strategies deal primarily with how animals handle toxins internally when consumed. It is impossible to separate outward grazing behavior from the internal consequences of eating, because digestive consequences affect the animals' propensity to eat particular plants (Provenza et al. 1992, Forbes 1998). Most published work on grazing herbivores was conducted with domestic livestock, and this review will reflect that bias. Research on wildlife will also be discussed where information is available.

Avoidance

It is clear that animals limit their consumption of poisonous plants at times (Table 3). How do animals

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Table 1. Direct and indirect economic losses from poisonous plants related to production and off take from domestic livestock and wildlife

<i>Direct losses</i>	<i>Indirect losses</i>
Death	Added fencing to restrict access
Wasting/reduced weight gains	Herding costs
Neurological incapacitation (horses)	Supplemental feeding
Abortions	Changes in grazing management
Weak/small offspring	Increased veterinary costs for treatment
Reduced fertility	Lack of immune response to vaccines
Birth defects	Lost opportunity to graze forage
Inability to sell/harvest animals	Lost nutrients in ungrazed forages
	Reduced land values
	Reduced value of grazing permits
	Herbicide costs for suppression
	Increased risk in overall enterprise

Table 2. Major plant toxins, herbivores and body system(s) affected, and examples of plants containing the toxin.

Toxins and subtypes	Animal Species Affected	Body System(s) Affected	Plants Containing Toxin	
			Common name	Scientific name
Alkaloids				
Diterpene	Primarily cattle; wildlife unknown	Paralyzes muscles	larkspur	<i>Delphinium</i> species
Pyrolizidine	Cattle, horses; deer	Liver toxin; photosensitization; wasting disease	groundsel	<i>Senecio</i> species
			houndstongue	<i>Cynoglossum officinale</i>
Steroidal (potato type)	Cattle, sheep, horses; wildlife unknown	CNS toxin; digestive tract	nightshades	<i>Solanum</i> species
Steroidal (veratrum type)	Sheep; mule deer unaffected	Birth defects; lung congestion	skunk cabbage	<i>Veratrum</i> species
			death camas	<i>Zigadenus</i> species
Piperidine	Cattle, sheep, horses; elk; presumably other wildlife also	CNS toxin; birth defects	poison hemlock	<i>Conium maculatum</i>
Quinolizidine	Sheep, cattle, horses; wildlife unknown	Respiratory paralysis; birth defects	lupine	<i>Lupinus</i> species
Indolizidine	Horses, cattle, sheep, elk, antelope, and possibly deer and other wildlife	Digestive, reproductive & CNS	locoweed	<i>Astragalus</i> and <i>Oxytropis</i> spp.
Glycosides				
cyanide glycosides	Cattle, sheep; wildlife unknown	Inhibits cellular respiration	chokecherry	<i>Prunus</i> species
			forage sorghums	<i>Sorghum</i> species
			arrowgrass	<i>Triglochin</i> species
coumarin glycosides	Cattle; wildlife unknown	Vit. K deficiency	sweet clover	<i>Melilotus</i> species
cardiac glycosides	Cattle, sheep, horses; wildlife unknown	acute heart toxin	milkweed	<i>Asclepias</i> species
			foxglove	<i>Digitalis</i> species
saponin glycosides	Cattle, sheep; wildlife unknown	digestive system	cow cockle	<i>Vaccaria pyramidata</i>
			corn cockle	<i>Agrostemma githago</i>
nitropropanol	Cattle, sheep; wildlife unknown	Respiration; CNS damage	milkvetch	<i>Astragalus</i> species
Isoflavones				
phytoestrogens	Sheep; quail, other wildlife unknown	Reproductive	clover	<i>Trifolium pratense</i>
			alfalfa	<i>Medicago sativa</i>
Oxalates				
	Sheep, cattle; wildlife unknown	Disrupts energy metabolism; possible hypocalcemia	halogeton	<i>Halogeton glomeratus</i>
			greasewood	<i>Sarcobatus vermiculatus</i>
			kochia	<i>Kochia scoparia</i>
Tannins	Cattle, horses, sheep; wildlife less affected	digestive system; kidney	oak	<i>Quercus</i> species
Terpenes	Cattle, sheep; bison also affected	CNS; reproductive system	ponderosa pine	<i>Pinus ponderosa</i>
			sagebrush	<i>Artemisia</i> species
			bitterweed	<i>Hymenoxys</i> species
			sneezeweed	<i>Helenium</i> species
Nitrates	Cattle, sheep; wildlife unknown	respiratory	pigweed	<i>Amaranthus</i> species

Table 3. Examples from research studies in which animals have preferred less toxic or nontoxic plant species or populations compared to more toxic species or populations¹

Plant species	Toxin	Animal species
Sudangrass <i>Sorghum sudanense</i>	cyanide	cattle
Sorghum <i>Sorghum vulgare</i>	cyanide	sheep & cattle
Sericea <i>Lespedeza cuneata</i>	tannin	sheep
Reed canarygrass <i>Phalaris arundinacea</i>	alkaloid	sheep
Lupine <i>Lupinus angustifolius</i>	alkaloid	sheep
Crotalaria <i>Crotalaria spectabilis</i>	alkaloid	cattle
Sagebrush <i>Artemisia tridentata</i>	terpenes	sheep
Bracken Fern <i>Pteridium aquilinum</i>	cyanide ²	sheep & deer
Blackbrush <i>Coleogyne ramosissima</i>	tannin	goats
Tall fescue <i>Festuca arundinacea</i>	alkaloid	cattle

¹ Adapted in part from Laycock 1978; for references contact the author

² Bracken fern contains other toxic compounds, but the study involved cyanogenic glycosides

“know” which plants are poisonous? Grazing animals may innately detect and avoid plant toxins (i.e., genetic mechanisms). Alternately, herbivores may learn about plant toxicity through digestive consequences (Provenza et al. 1992).

Innate avoidance

Herbivores use taste and odor to detect and avoid poisonous plants (Provenza et al. 1992). Sweet flavors in plants often indicate carbohydrates (i.e., calories), whereas bitter flavors hint that toxins are present (Garcia et al. 1974). Some argue that animals are genetically programmed with knowledge about plant palatability, and for that reason animals are attracted to sweet flavors and repelled by bitter flavors (Owen 1992). This implies that even inexperienced grazing animals should avoid toxic plants (Fowler 1983) but, this does not appear to be the case for most interactions of herbivores with toxic plants. For example, naive animals are often most susceptible to poisoning (Provenza 1997). Grazing animals also eat some toxic plants with strong odors (e.g., pine needles) even when other forage is available (Pfister and Adams 1993). Furthermore, evidence of innate toxin recognition is lacking.

Many toxins supposedly taste bitter (e.g., alkaloids, saponins, cyanogenic glycosides), have offensive odors (e.g., terpenes) or provoke an astringent sensation when eaten (e.g., tannins). However, bitterness is not universally repellent (Glendinning 1994) and some toxins do not have a bitter taste (e.g., alkaloids; Molyneux and Ralphs 1992). Sheep (Arnold and Hill 1972), cattle (Pfister et al. 1996), and guinea pigs (Nolte et al. 1994) do not necessarily avoid bitter tastes, nor do sheep form stronger aversions to bitter than to sweet flavors (Launchbaugh et al. 1993). Furthermore, animals acquire

preferences for bitter and sour flavors when consumption is followed by calorie enhancement even when these flavors were not initially preferred (Sclafani 1991). In fact, some foods, like coffee and chocolate, are highly desired by many humans precisely because of their bitter taste (Zellner 1991). It seems clear that animals are not, in the main, inherently deterred by the supposed bitterness or other detected quality of plant toxins.

Learning through consequences

When grazing animals reject toxic plants in favor of less toxic alternatives (e.g., Table 3), learning is usually involved. Provenza (1995) recounted how goats introduced to blackbrush ranges initially ate current season's growth, yet within 4 hours goats shifted consumption to less nutritious older growth. Goats apparently avoided the more nutritious current season's growth because it contained a larger proportion of tannins that adversely affected the animals. If Provenza and colleagues had not observed the goats' initial diet selection, they would have continued to assume that goats never ate current season's growth.

Domestic livestock losses attest that learning is not a perfect avoidance mechanism (Provenza et al. 1992). However, learning is still a useful means by which most livestock survive grazing ranges with poisonous plants, as with larkspurs (Pfister et al. 1997). Wildlife survival, when interacting with toxic plants, is probably due primarily to other attributes such as tolerance or detoxification (Fowler 1983). Wild herbivores may not need to learn to avoid toxic plants if they usually suffer little harm (Nichol 1938).

How do animals learn which plants to eat and which to avoid? The answer lies in the concept of

postingestive consequences (Provenza et al. 1992) and learned aversions (Garcia 1989) or preferences (Booth 1985). Provenza and colleagues have clearly shown the importance of aversive conditioning in diet selection (see Provenza, this volume), and these principles apply to the selection of toxic plants (Provenza et al. 1992, Provenza 1995, Howery et al. 1998). Four major types of learning are relevant to feeding strategies and toxic plants: (1) learning by offspring in the womb; (2) learning from mother; (3) social learning; and (4) trial-and-error learning.

Aversive conditioning. Postingestive consequences (or feedback) are signals from the gut to the brain telling the animal what effect the food is having; in the case of calories, the effect is positive; in the case of toxicity, the effect is negative (perhaps nausea or some other adverse feeling commonly termed malaise). Conditioned flavor aversions occur when negative feedback signals the animal that the ingested plant is having (or recently had) a negative (i.e., toxic) impact. When this occurs, the animal makes the unconscious association between plant flavor (taste and/or odor) and negative digestive feedback. In future encounters, the plant becomes less preferred by the animal (termed a hedonic shift) because of the past negative association. Flavor aversions occur subconsciously, but the sight and smell of the plant are inextricably linked with the negative feedback such that the plant is avoided in subsequent encounters. Thus, animals make diet choices that result from past experiences with the plant, both positive and negative. Positive feedback results in animals seeking out particular plants (e.g., "ice-cream plants"), whereas negative feedback causes animals to avoid specific plants (Provenza 1996).

Aversive conditioning has been shown with several plant toxins, including alkaloids, tannins, cyanogenic glycosides, terpenes, and glucosinolates (Provenza et al. 1992). Conditioned food aversions may be mild (i.e., temporary) or strong (i.e., permanent) depending on the toxin dose and when and how the toxin affects the gut and brain. The toxin must generally be sensed in the brain 4 to 12 hours after eating the plant for an aversion to occur, and stronger aversions are conditioned by a shorter delay between consumption and toxic effect. Therefore, aversions rarely develop if the toxin acts very slowly over days and weeks (e.g., pyrrolizidine alkaloids in senecio or indolizidine alkaloids in locoweed). Furthermore, the toxin must activate the emetic center in the brain that controls nausea and vomiting to condition an aversion. One cannot expect an aversion from toxins like strychnine that do not affect the emetic center. As will be discussed later, aversive conditioning may be employed to keep livestock from eating poisonous plants such as larkspur (Ralphs 1997) or locoweed (Ralphs et al. 1997).

Learning in the womb. Grazing animals may actually be born knowing something about which plants are "good" or "bad" because learning occurs while offspring are still in the womb. In humans (Mennalla and Beauchamp 1997), rats (Smotherman 1982a) and sheep (Nolte et al. 1992, Schaal and Orgeur 1992) *in utero* exposure to flavors in amniotic fluid may contribute to subsequent preferences for such flavors. Taste and odor aversions in young animals can also be conditioned *in utero* (Stickrod et al. 1982, Smotherman 1982b). The impact of plant toxins eaten by pregnant animals may be very destructive to fetal development (Panter et al. 1992), but little is known about how toxins that pass the placental barrier influence subsequent diet selection in the offspring.

Learning from mother: milk and model. Learning from mother has a major influence in the selection of toxic plants, and can be indirect (through milk flavors) or direct (i.e., modeling). Mothers' influence can occur indirectly because of tastes passed through milk to nursing young. Experience with a strong flavor in milk predisposes lambs to eat more of a food with that flavor later in life (Nolte and Provenza 1992). Many toxins can be passed to the nursing young via milk (Panter and James 1990), but it may be difficult to avert suckling animals to mother's milk from toxin-induced illness because milk is usually a very safe food.

Young animals learn from their mother's example to eat preferred foods and avoid foods with toxins (Provenza et al. 1992). Using lithium chloride as an artificial toxin, Provenza and colleagues found that lambs learned to avoid novel foods that their mothers were conditioned to avoid (Mirza and Provenza 1990, Thorhallsdottir et al. 1990a, b). Conversely, animals learn what to eat by mimicking their mother, even if the plant is toxic. Nursing calves began to eat substantial quantities of locoweed (Pfister unpublished observations) and low larkspur (Pfister and Gardner 1999) on the same day as their grazing mothers, suggesting that calves mimicked their mothers' diet. Mother's influence does, however, have its limits. Young lambs avoided a plant paired with a toxin whether or not their mother ate the plant (Provenza et al. 1993). Calves that initially ate larkspur with their mothers sharply curtailed consumption a few days later (Pfister and Gardner 1999), perhaps because of adverse feedback (Pfister et al. 1997). Though mother is an important source of information for young animals, postingestive consequences are probably more important (Provenza et al. 1993).

Others social influences. Dietary social facilitation is the influence one grazing animal exerts on the diet selection of another. Domestic livestock, in particular,

are social animals and they frequently observe one another and modify their diet selection based on what their grazing companions are eating (Thorhallsdottir et al. 1990a, Ralphs et al. 1994). Cattle eating locoweed (Ralphs et al. 1994) and larkspur (Lane et al. 1990) have influenced other animals to eat these toxic plants.

Learning by trial-and-error. Grazing animals learn about poisonous plants through cautious sampling of both familiar and novel foods (Provenza et al. 1992). As toxic plants grow and mature, they often change in nutritive composition and toxicity (Pfister et al. 1994). Because the quality and quantity of forage often varies both spatially and temporally, animals may be highly motivated to sample foods and monitor food resources (Wang and Provenza 1997, Day et al. 1998). Sampling is however an imprecise process and errors made while sampling toxic plants may be debilitating or lethal (Provenza et al. 1992). Trial-and-error learning is risky, but sampling usually involves eating only small amounts of a food, so the potential for toxicity is reduced.

One risk-reducing behavior analogous to cautious sampling is neophobia, in which animals are reluctant to eat much of novel foods (Burritt and Provenza 1989, 1991; Provenza et al. 1995). Animals may be particularly reluctant to eat novel foods with strong flavors (Augner et al. 1998). When grazing animals experience negative feedback from toxins or positive feedback from sampling foods, they usually associate such feelings with novel rather than familiar flavors (Burritt and Provenza 1989).

Mixed Diets

Grazing animals usually select diets composed of many plant species. This may simply reflect the continuous sampling mode of herbivores (Day et al. 1998), or it may also reflect attempts to limit ingestion or impact of plant toxins (Provenza 1996, Launchbaugh 1996). A basic principle of toxicology is "the poison is in the dose" - in other words, many toxins exhibit a dose-response curve, where little or no toxicity is displayed at low doses and increasing doses produce more severe symptoms. Plants with toxins also contain varying kinds and amounts of nutrients. Thus, diet selection with toxic plants is always a tradeoff between nutrition and toxicity (Freeland and Janzen 1974, Freeland 1991, Provenza 1996). Freeland and associates demonstrated that animals can decrease the toxic effects of a single plant by eating a mixture of plants containing different toxins (Freeland et al. 1985, Freeland and Saladin 1989). Mule deer were able to eat about twice as much sagebrush and juniper together than when each was fed alone (Smith 1959), suggesting that the ruminal microflora in deer could handle plant secondary compounds from different sources better than from a

single source. Besides positive feedback from nutrients, learning may be facilitated by a "medicine effect," wherein the negative effects of ingesting one plant may be ameliorated to some extent by eating another plant. Eating a mixed diet may therefore be the equivalent of self administration of antidotes (Freeland 1991).

Not only is the amount eaten important, but ingestion rate may also be important to allow sufficient time for detoxification to occur (Foley et al. 1995, Foley et al. 1999). Detoxification occurs through several pathways depending on the specific toxin and animal (Smith 1992). Thus, mixing foods in a nonrandom manner facilitates consumption of more food, including foods with toxins (Freeland 1991).

Cyclic and Intermittent Consumption

Grazing animals can avoid toxicoses by limiting their consumption of a specific toxic plant each day. Alternatively, animals might vary toxic plant consumption from day-to-day to limit potential cumulative effects of specific toxins. Grazing studies with tall larkspur suggested that consumption above 25 to 30% of the diet for 1 or 2 days led to reduced consumption on subsequent days (Pfister et al. 1988). In pen studies, cattle responded to larkspur dosing with distinct cycles of food intake such that 1 to 3 days of higher consumption was followed by 1 to 3 days of reduced consumption (Pfister et al. 1997). We noted that larkspur had a dose-response threshold of 14 to 18 mg toxic alkaloid/kg body weight, and periods of reduced consumption below this threshold probably allowed animals time to recover from the larkspur-induced illness. Sheep adjusted intake of LiCl according to the toxin concentration in foods when the concentration varied greatly (Wang and Provenza 1996, Launchbaugh et al. 1993).

How might grazing animals become temporarily averse to a single plant and vary consumption of this plants? First, when illness follows a meal dominated by a toxic plant, grazing animals apparently can make the connection between the dominant food and the subsequent illness. Goats acquire an aversion to the food eaten in the greatest amount when poisoning follows a meal of novel foods (Provenza et al. 1994). In the case of larkspur, cattle eat large amounts during some grazing bouts (Pfister et al. 1988). Second, the strength of the plant flavor may be important (Augner et al. 1998). If a plant flavor is strongly correlated to the amount of toxin, grazing animals can regulate intake of the plant based on the strength of the flavor (Launchbaugh et al. 1993). Plus, re-experiencing the flavor during rumination may help the animal associate that flavor with illness that may last for several hours after ingestion. Third, previous

experience with a plant, and certainly prior illness associated with eating a toxic plant, may signal animals to stop eating the plant. Lambs avoid the food that made them ill in the past when poisoning follows a meal of several foods (Burrill and Provenza 1991). Finally, limited intake of toxic plants may result from temporary aversions. Provenza (1996) has proposed that varied diets result from temporary aversions in which excesses of toxins and nutrients likely interact to partially regulate sampling and diet selection within a meal.

Why do animals return to eat a plant that has been aversive in the past? Animals begin sampling forages because ingestion of small amounts usually causes no or few negative effects. In addition, many toxic plants contain substantial nutritional value (larkspur: Pfister et al. 1989; locoweed: Ralphs and Molyneux 1989) and provide positive digestive feedback. Both locoweed and plains larkspur contain more than 20% crude protein early in the spring (Pfister unpublished observations). Eating some of a toxic plant provides needed nutrients with little toxicity, but increased consumption results in heightened adverse effects because of the dose-response characteristic of many toxins. Partial avoidance or partial preference (Day et al. 1998) for a toxic forage would likely result in a grazing animal eating variable but increasing quantities of the forage, until negative feedback (or alternatively excess of nutrients; Provenza 1996) became sufficiently strong to temporarily drive the animal "off" the feed (e.g., larkspur; Pfister et al. 1997). Each time a toxic forage is eaten without negative consequences, the aversion is weakened and will eventually vanish without additional negative feedback (Lane et al. 1990, Ralphs and Stegelmeier 1998).

Eject the Toxin

Once a toxin is eaten, it is in the animals best interest to quickly get rid of it. This usually occurs through vomiting or diarrhea (Kingsbury 1983). Although we don't normally think that ruminants or horses vomit, this reflex is common in mammals (except rodents). Sheep, goats, and cattle can and will vomit in response to eating toxins (Mullenax et al. 1966, Buck et al. 1966, Oehme and Barrett 1986). In livestock, vomiting is problematic because animals can aspirate the gut contents into their lungs, which can be fatal. Vomiting in ruminants is apparently sensitive to dose, as some toxic plant doses resulted in vomiting, whereas higher doses produced severe retching (Mullenax et al. 1966). Horses probably do not vomit except when near death, but commonly experience diarrhea (Oehme and Barrett 1986). Diarrhea aids in rapid elimination of toxins from the gut before absorption. In some episodes of diarrhea, there is a decrease in intestinal motility, thus reducing the

absorption of the toxin through reduced gut motility (e.g., cyanide).

Complex, Degrade, or Detoxify

Much has been written about animals' abilities to detoxify substances in plants. For excellent reviews see Freeland and Janzen (1974), Allison (1978), McArthur et al. (1991), Smith (1992), Launchbaugh (1996), and Cheeke (1998). Animals may complex toxins in the mouth and/or the gut, degrade the toxin in the gut via microbial action, or absorbed toxins may be detoxified by various reactions in either the stomach wall or the liver. Without these detoxification systems operating effectively, animals would probably not be able to eat any plant toxins (Jason and Murray 1996).

Complex in mouth or gut

Complexes formed in the mouth may provide protection from effects of plant toxins. Animals that have evolved eating tannin-rich shrubs secrete proline-rich proteins (PRPs) in their saliva which bind to tannins (Robbins et al. 1991). Interestingly, salivary proteins from generalist herbivores like bear and deer bind several tannins, whereas proteins from specialist feeders like moose and beaver bind only the tannin most commonly found in their diet (Hagerman and Robbins 1993). Tannin-containing diets did not induce PRP production in sheep (i.e., grazers), whereas deer (i.e., browsers) previously exposed to tannins produced saliva with PRPs when reexposed. The saliva-tannin complex essentially inactivates tannins and reduces absorption and toxic effects.

Other activity in the mouth and nose may facilitate survival when eating toxic plants. Cheeke (1998) speculated that detoxification activity in the mouth might allow animals to ingest some plants with very noxious odors, such as sagebrush. Many terpenes are lost through volatilization during chewing as when pygmy rabbits eat sagebrush (White et al. 1982). Increased chewing and ruminating has also been associated with increased sagebrush consumption in sheep (Fraker and Launchbaugh, abstract in this volume). Further, nasal tissue is capable of detoxifying some toxins through induction of the P450 enzyme system. Goats and sheep will eat pyrrolizidine alkaloid-containing plants such as tansy ragwort which is toxic to larger animals such as cattle. The inducible presence of a nasal detoxification system might facilitate the consumption of the noxious-smelling tansy ragwort by goats and sheep (Cheeke 1998).

Some plant toxins are bound (sequestered) with

other eaten material to prevent toxic actions (Smith 1992). Geophagy (i.e., eating soil) is common among ungulates (Jones and Hanson 1985). Despite the widespread belief that mineral licks are sought by animals for their sodium content, it is more likely that other minerals (e.g., Ca) are more important (Jones and Hanson 1985). An early description of an Illinois mineral lick described it as "soft, salt[y] and sulphurous" (Jakle 1969). Detoxification using sulphur is metabolically expensive and sulphur is usually in short supply (Brattsten 1979, McArthur et al. 1991). Thus, animals might practice geophagy to enhance sulphur in the diet. Moreover, mineral licks are often high in various clays (Jones and Hanson 1985) and some clays naturally bind to various toxins (Smith 1992). Therefore, geophagy may help deactivate plant toxins.

Gut degradation by rumen microbes

Ruminants may have a significant evolutionary advantage over nonruminants when dealing with plant toxins because of their large forestomach that dilutes and may degrade or detoxify certain plant toxins (Table 4; Oehme and Barrett 1986, Smith 1992). The nearly neutral pH of the rumen environment may modify the plant toxin, or by virtue of the large volume (60-70 gal) the toxin may be immediately diluted. Of great significance for ingestion of toxic plants is the massive numbers of microbes in the rumen, where millions of microbes may be found per milliliter of rumen contents. Certain microbes are capable of degrading or detoxifying some plant toxins. In some cases, however, rumen microbes can convert innocuous substances into toxic compounds (Table 4, Allison 1978). Generally for a rumen microbe to degrade a toxic plant compound, utilization of the compound must yield energy for the microbial population, and the microbial population must inhabit a particular rumen niche that allows it to survive when the toxin is not present, and expand the population rapidly when the toxin enters the rumen (Weimer 1998).

Once plant toxins are absorbed from the gut into the blood, they are often transported to the liver (hepatic tissue). All nonpolar foreign compounds are potentially toxic. Therefore, one of the first tasks for the body is to change these nonpolar (i.e., lipid-soluble) substances to polar compounds (i.e., water-soluble) so they can be excreted in urine. If left unchanged, they would ultimately poison the body. Therefore, the liver contains enzyme systems that metabolize (or alter) nonpolar compounds so that they can be excreted. Although most of the metabolic conversion of plant toxins occurs in the liver, cells in the kidney, intestinal mucosa, lungs and skin may also be involved (Zimmerman 1978). There are several advantages to liver detoxification vs. microbial

degradation (Foley et al. 1999): (1) liver enzymes are under genetic control, so some protection can be passed to offspring; (2) there is much variability in enzyme system activity, so these enzymes can handle a variety of toxins; and (3) liver enzymes are rapidly inducible (i.e., can be jump started and the amount of enzyme elevated within hours if necessary).

The nutritional state of the animal and dietary nutrients are major factors in toxin intake, as detoxification requires nutrients and energy to alter toxins and maintain acid-base equilibrium (Jessop and Illius 1997, Foley et al. 1999). For example, low protein diets decrease detoxification activity in the liver (e.g., cytochrome P450 enzyme system; McLean and McLean 1969). In the case of tansy ragwort alkaloids, pretreatment of animals with the alkaloid jacobine results in elevated detoxification activity of pyrrolizidine alkaloids (Miranda et al. 1980). Antioxidants that promote detoxification also provide protection against bitterweed (Cheeke 1998).

Tolerance

Some species or individuals are more tolerant to toxic plants than others. The enzymatic ability of the liver varies greatly between animal species. For example, sheep can tolerate more pyrrolizidine alkaloids (PAs) than cattle. Part of the detoxification occurs in the gut by microbes (Craig et al. 1992), but liver metabolism is more important (Cheeke 1994). It is also possible that differences in activity at receptor sites account for tolerance in some animals. Likewise, it took 5 times more tall larkspur to poison sheep compared to cattle (Olsen 1978), and the tolerance of sheep was thought to be due to differences in ruminal metabolism. Recent studies indicate, however, that sheep nicotinic acetylcholine (nACh) receptors bind the larkspur toxins much less avidly than do cattle nACh receptors, thus accounting for the species difference (Stegemeier, unpublished data).

Microbial adaptations in the gut, detoxification in the gut wall or liver, and receptor site responses can be induced by consumption of plant toxins. Eating small quantities of some plant toxins may thus provide an opportunity for the animal's system to adapt to the toxin. Nonetheless, tolerance does not develop to all toxins. The effects of many toxins are cumulative (e.g., bracken fern, pyrrolizidine-alkaloid containing plants), and animals get progressively more poisoned as they continue to ingest the material.

Very little is known about tolerance of wildlife species for plant toxins (Table 5). Because of their experience and history, native wildlife on rangelands are

Table 4. Examples of ruminal or postruminal detoxification and toxification of plant secondary compounds

Toxin	Plant Species	Degradation mechanism
Detoxification: degradation of toxins by microbes and postruminally		
Oxalates	halogeton greasewood	oxalic acid metabolized by <i>Oxalobacter formigenes</i> ; ruminants can adapt to remarkably high concentrations
Cyanide	chokecherry sorghum	cyanide oxidized by sulphur donors to yield thiocyanate
Pyrrolizidine alkaloids	senecios houndstongue	Possibly ruminal degradation in sheep and goats, more likely high rate of pyrrole conjugation in liver.
Mimosine	<i>Leucaena</i>	mimosine converted to toxic DHP; the bacteria <i>Synergistes jonesii</i> metabolizes DHP to nontoxic compound
Estrogens	clover	cattle may metabolize estrogens more efficiently than sheep; or cattle may have different receptors than sheep
Miserotoxin	milkvetch	several ruminal bacteria degrade NPOH; diet dependent; reduced absorption of modified NPOH from gut
Essential oils	fir trees sagebrush	ruminal degradation after adaptation
Toxification: production of toxins by microbes or postruminally		
Pyrrolizidine alkaloids	senecios houndstongue	alkaloids metabolized in liver to toxic pyrroles, especially in cattle; small ruminants much less affected (see above)
Nitrates	forage sorghum	nontoxic nitrates reduced to toxic nitrite in rumen; adaptation in the rumen can occur quickly and decrease nitrite toxicity
Miserotoxin	milkvetch	hydrolysis and release of NPOH, followed by enzymatic oxidation to very toxic NPA
Cyanide	serviceberry	hydrolysis of glycoside results in release of toxic cyanide
Estrogens	clover	sheep more susceptible; may have more sensitive receptors, may metabolize isoflavones to more toxic equol

thought to be more tolerant of toxic plants than livestock introduced into pastures with poisonous plants (Arnold and Hill 1972, Laycock 1978). When offered various plants, deer avoid many, but not all, toxic plants (Nichol 1938, Longhurst et al. 1968, Jessop et al. 1986) and those that they do eat may do little harm (Nichol 1938).

An Addictive Proposition

Addiction generally refers to an animal's craving for a particular plant or compound. Psychologists use the term "self-administration" to describe the behavior of animals seeking a particular plant or substance due to positive reinforcement (i.e., a chemically-enhanced sense of well being in the pharmacological sense, not the nutritive sense). Siegel (1979) identified 122 well-documented cases where mammals had self-administered a plant for CNS stimulation; most of the animals were herbivores (41% domestic and 59% feral). There have been numerous accounts of addiction in livestock grazing on range plants. Many alkaloid-containing plants have been regarded as addictive (Siegel 1979): buttercup, nightshade, laurel, rhododendron, and oak. Panter (personal communication) related that pigs fed fresh poison hemlock apparently became addicted to the flavor. The most famous of the "addictive" plants is locoweed (Lewin 1931). The German toxicologist Lewis

Lewin (1931) described livestock addiction to locoweed by declaring that "animals refuse to take any other kind of food and greedily seek to procure their old fodder, like the morphinist his morphia." He also described animal addictions to the Australian plant *Swainsona*, long before it was known that *Swainsona* and locoweed contain the same toxin, swainsonine. Marsh (1909) also noted that locoweed was addicting to various animals, including mules, pigs and antelope.

Are addictions important in ingestion of toxic plants? It is likely that animals sometimes self-administer toxic plants for the pharmacological effects (Siegel 1979). Is locoweed addictive? Ralphs et al. (1990) reported that dried, ground locoweed was not addictive, but animals did habituate or become accustomed to eating the plant material. Many drugs (and all plant toxins are drugs) can have positive pharmacological effects but not cause addiction (Marinelli et al. 1998). Dose also is important, as drugs like methamphetamine can provide positive reward at low doses, and be aversive at higher doses (Cabib et al. 1996). Presently there are no clear answers about the addictive or rewarding capabilities of locoweed or other toxic plants. Positive reinforcement would increase the probability that animals continue to eat toxic plants under some circumstances.

Table 5. Examples of wildlife species in the U.S. where the animals apparently tolerated or detoxified the toxin once ingested, or alternatively, cases where intoxication resulted from ingesting a poisonous plant. In virtually all cases, the mechanism(s) is not known.

Animal Species	Toxic plant	
	Scientific name	Common name
Tolerate or Detoxify		
Mule deer	<i>Astragalus</i> spp.	locoweed
Mule deer	<i>Pteridium</i> spp.	bracken fern
Mule deer	<i>Psoralea</i> spp.	elk clover
Mule deer	<i>Artemisia</i> spp.	sagebrush
Black-tailed deer	<i>Pseudotsuga menziesii</i>	Douglas fir
Black-tailed deer	<i>Senecio jacobaea</i>	tansy ragwort
White-tailed deer	<i>Kalmia latifolia</i>	laurel
White-tailed deer	<i>Rhododendron maximum</i>	rhododendron
Pronghorn antelope	<i>Astragalus emoryanus</i>	peavine
Pronghorn antelope	<i>Senecio longilobus</i>	threadleaf grousel
Pronghorn antelope	<i>Psilostrophe tagetina</i>	woolly paperflower
Pronghorn antelope	<i>Artemisia nova</i>	black sagebrush
Pronghorn antelope	<i>Artemisia tridentata</i>	big sagebrush
Elk	<i>Pinus ponderosa</i>	ponderosa pine
Moose	<i>Amelanchier</i> spp.	serviceberry
Moose	<i>Prunus</i> spp.	
Intoxicate		
White-tailed deer	<i>Sorghum vulgare</i>	sorghum
White-tailed deer	<i>Crotalaria spectabilis</i>	crotalaria
Pronghorn antelope	<i>Fluorensia cernua</i>	tarbush
Pronghorn antelope	<i>Prunus</i> spp.	chokecherry
Pronghorn antelope	<i>Astragalus</i> spp.	locoweed
Sika deer	<i>Pinus banksiana</i>	jack pine
Elk	<i>Oxytropis sericea</i>	whitepoint locoweed
Elk	<i>Conium maculatum</i>	poison hemlock
Bison	<i>Pinus ponderosa</i>	ponderosa pine
Feral horses	<i>Oxytropis</i> spp.	locoweed

Management Implications

Prospects for and problems with aversive conditioning

Many livestock producers are interested in using aversive conditioning to reduce domestic livestock losses to some poisonous plants (e.g., larkspur, locoweed, pine needles). As detailed by Ralphs and Provenza (1999), it is relatively easy to avert an animal to some poisonous plants using the emetic drug, lithium chloride (LiCl). Procedurally, livestock are placed into a corral in small groups, fasted for 12 to 48 hrs, offered freshly-harvested plant material, and observed to verify that they have eaten at least a few bites of the plant. As quickly as possible, the animals are given a dose of LiCl mixed with water (for cattle: 200 mg/kg; for sheep: 150 mg/kg) via a stomach tube. The LiCl acts quickly to make the animal nauseous. Thus, the animal will associate the taste of the plant with the illness and avoid the plant in future encounters. Averted cattle have avoided tall larkspur (Ralphs 1997), locoweed (Ralphs et al. 1997), and pine needles (Pfister 1999) in pen and field studies.

There are several potential pitfalls to using this technique (Ralphs and Provenza 1999). The most serious concern is that averted animals *must* be grazed separately from non-averted companions, or the aversion will be extinguished by the influence of social facilitation (Lane

et al. 1990). The aversion is more persistent if animals are naive to the target plant; experienced animals can be averted, but it may take several pairings of taste and illness (Ralphs and Provenza 1999). An aversion conditioned to one plant species or form of the plant may not be generalized to another. For example, cattle averted to one species of larkspur did not avoid another species when the plants grew together (Ralphs, unpublished observations). Cattle averted to green pine needles extinguished the aversion after eating grass mixed with dried needles (Pfister 1999). Partial or temporary aversions will not be effective on rangelands (e.g., Houpt et al. 1990) as only complete avoidance will persist over a relevant time scale (i.e., months or years; Lane et al. 1990, Ralphs and Stegelmeier 1998, Pfister 1999).

Averting large numbers of animals requires extraordinary efforts by livestock producers (Ralphs and Provenza 1999). Producers may begin by averting only replacement heifers, but these animals will require special grazing management consideration thereafter. There is considerable stress placed on averted animals from the extensive fasting that may be required to induce initial consumption of a novel plant. Additional stress is placed on averted animals from the 2 to 3 day illness induced by LiCl, including profuse diarrhea and weight loss. Averting lactating cows may be problematic because of potential impacts on the calves. Overdosing or mishaps when dosing LiCl can be fatal to cattle. Nonetheless,

producers with substantial and sustained losses, or those with small herds, should consider aversive conditioning as part of an overall solution to poisonous plants.

Other implications of social facilitation

Social facilitation has important implications for management of grazing animals, even if livestock producers are not involved in aversive conditioning. Grazing animals eating toxic plants can influence either their calves or other companions to eat the plant. Young animals may be especially prone to follow their mother because of their close social proximity, tendency to mimic mother, and flavors experienced in the milk. Grazing animals with a proclivity to eat toxic plants should be identified and removed from the herd in some circumstances. Some producers in New Mexico with locoweed-infested pastures have systematically, over the several years, removed any cow from their herds seen eating locoweed, before she either becomes intoxicated or influences her calf or companions to eat locoweed. This "loco pull" strategy, combined with a recuperation period (if needed), has proven to be a better economic choice than doing nothing, or selling noticeably poisoned animals (Torell et al. 1999). Of course, this approach will not work with all toxic plants, but is worth considering for plants with chronic (i.e., slow) toxicity such as locoweeds, pine needles, groundsels, and snakeweed.

Manipulating diet selection- for good or for ill

It is axiomatic that producers can sometimes reduce ingestion of poisonous plants by maintaining rangelands in good forage condition and avoid even temporary overutilization of ranges. Many toxic plants are not highly preferred when offered in a mix with other desirable forages (Taylor and Ralphs 1992). Even if animals eat small amounts of many poisonous plants, they will suffer few ill effects if other nontoxic forage makes up the majority of their diet. Taylor and Ralphs (1992) documented how proper grazing management, stocking rates, and mixed species grazing can decrease losses to poisonous plants in Texas. Even so, the more intensive the grazing management practices, the greater the likelihood for error, and management errors may contribute substantially to losses of domestic livestock. Producers in northern Utah graze cattle each summer on high elevation ranges in the Raft River Mountains. For many years, the producers used a rest rotation grazing system, wherein 3 pastures were grazed in sequence, and 1 pasture was rested each summer. Range condition improved yet annual losses to locoweed exceeded 20% (Ralphs et al. 1984). Based on observations that most consumption of locoweed occurred during August (i.e., after flowering), the grazing season was cut back from 71

to 47 days, while increasing cattle numbers, and the grazing system was altered to a Merrill 3-herd, 4-pasture system (Ralphs et al. 1984). These simple changes altered diet selection, as cattle were no longer forced to select locoweed, and shortened the exposure to locoweed when it was most palatable. As a result, yearly losses declined to about 3%.

Animal managers should be cautious about exposing naive animals to unfamiliar rangelands with toxic plants. Animals that are driven or trucked into a pasture may be hungrier or thirstier than normal, and may then accept toxic plants they would otherwise reject. As many as 1,200 sheep were lost at one time when hungry bands were released into halogeton-infested rangelands. Ironically, sheep can tolerate large amounts of the toxic oxalates if given time for ruminal adaptation. Naive animals placed in strange surroundings will probably reduce intake (i.e., neophobia) and increase exploratory behavior (Provenza 1997). Because most plants may be unfamiliar, grazing livestock are likely to increase their intake of toxic plants, and losses may be severe.

Nutritional stress may contribute to losses from poisonous plants. Animals that are not well nourished may be less able to detoxify plant toxins, thus the threshold for a lethal dose may decrease. Further, diet selection may expand to include some less palatable toxic plants when livestock are undernourished or hungry. Malnourished livestock may learn to eat less of a plant toxin if the adverse postingestive consequences are magnified by poor body condition and decreased detoxification abilities (Launchbaugh 1996). However, because an animal in poor body condition may have a lower threshold for a toxin, the initial exposure may kill the animal, before learning can occur.

Animals' perceptions of toxic plants differ when starved or deprived, as hungry deer eat some toxic plants that are rejected when forage is sufficient (Longhurst et al. 1968), and lambs are less discriminating when hungry (Wang and Provenza 1996). Nonetheless, pen-fed deer will starve before eating some toxic plants (Forbes and Bechdel 1931). Grazing livestock, when hungry, will also eat toxic plants that they reject in other circumstances (Merrill and Schuster 1978). As many poisonous plant researchers can attest, it is also common for pen-fed livestock to starve before eating some plants that are suspected of being toxic (Kingsbury 1983, Pfister personal observations). Hungry cattle ate progressively less larkspur as rumen fill decreased, suggesting that hunger *per se* provided little motivation to eat larkspur (Pfister et al. 1988). Further, poorly-fed animals may be more susceptible to some toxic effects (James et al. 1975).

Supplementation

Strategic supplementation of limiting nutrients may alleviate some toxic plant problems. The supplement can provide nutrients (e.g., protein) that will change diet selection, and further provide nutrients to enhance detoxification capabilities. If livestock show a pattern of selecting a particular toxic plant during a portion of the grazing day, offering a supplement at that time of day can disrupt grazing behavior (Adams 1985) and possibly reduce toxin intake.

Several dietary additives can potentially ameliorate the adverse effects of tannins or terpenes, including polyethylene glycol (PEG), activated charcoal, and calcium hydroxide. PEG has a high binding affinity for tannins, and has been shown to increase intake of tannin-rich forage (Silanikove et al. 1994). Intake of tannin-rich foods is probably increased by PEG because binding the tannins with PEG may alleviate adverse postingestive consequences such as lesions in the gut. Activated charcoal has recently been shown to increase intake of terpene-rich bitterweed (Scott, unpublished). Further, activated charcoal fed to lambs increased intake of big sagebrush by 40% compared to control lambs (Banner et al. 1999). A supplemental ration containing 10 to 15% calcium hydroxide has been used with some success to reduce oak toxicity to ruminants (Dollahite et al. 1966).

Conclusions

Most domestic or wild ungulates that graze on rangelands with poisonous plants do not succumb to these plants. Animals are able to cope with poisonous plants using both behavioral and physiological adaptations. Behavioral mechanisms converge on postingestive feedback and aversive conditioning, as animals learn which plants cause illness. Physiological mechanisms center on detoxifying plant compounds in the gut by rumen microbes or in the liver through enzymatic reactions that allow toxins to be excreted. Domestic livestock are more often made ill or killed by toxic plants than are wild ungulates, probably because wild animals have more developed avoidance or detoxifying capabilities than do livestock. Finally, some domestic livestock and many wildlife losses to poisonous plants result from human interventions that override coping strategies.

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