Integrating Plant Secondary Metabolites and Foraging Behavior to Enhance Animal Health in Ruminant Production Systems

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Abstract. Legumes and forbs contain bioactives or plant secondary compounds (PSC) with potential to enhance animal health through their antibiotic, antioxidant and immunomodulatory properties that are evident even at small dietary concentrations. In turn, ruminants can regulate their ingestion of PSC through behavioral mechanisms that allow for the efficient achievement of homeostasis. High concentrations of PSC lead to food avoidance, whereas lower content of PSC in the diet achieved through regulatory mechanisms of ingestion could promote medicinal and/or prophylactic effects in the animal and concomitant health benefits to milk and meat products. Under this context, we discuss the restructuring of rangelands and pasturelands through the strategic distribution of legume- and forb-rich patches in monotonous landscapes dominated by grasses, thus re-establishing their functionality. Such strategies can synergistically complement and provide new dimensions (prophylactic-medicinal, product quality) to the forage resources already available to livestock.

Introduction

Rangelands and pasturelands provide herbage for ruminant production systems worldwide and are a source of high-quality edible protein and cash income from non-arable lands (Varijakshapanicker et al. 2019; Adesogan et al. 2020). These resources can help producers maintain profitable operations while addressing growing consumer demands for environmentally, economically, and socially sustainable food (Sanderson et al. 2007; Villalba et al. 2019). Historically, cattle evolved in the Mediterranean region grazing a diverse palette of broadleaf forb and grass species (Grove and Rackham 2001), but most cowherds grazing rangelands today consume a diet dominated by a monotony of grasses, from improved species in monocultures to weeds that invade degraded landscapes (Paterson et al. 2001; Robins et al. 2020). In addition to the declining nutritional value of these forages as they mature, diets are typically devoid of functional biochemicals or plant secondary compounds (PSC) that are fundamental for animal health and the neutraceutical properties of their products (e.g., meat and milk) (Van Vliet et al. 2021).

Plant secondary compounds, such as phenolics, terpenoids, and alkaloids generally present in woody species, legumes and forbs were long regarded as waste products of plant metabolism, ever since they were identified in the second half of the 19th century (Sachs 1873; Hartman 2008). Since then, many different roles have been recognized for these chemicals, including their indispensable involvement in the survival strategies of plants (Hartman 2007), most notably as plant defense against herbivores (Palo and Robins 1991), and more recently as key players in the primary metabolism of plants (Erb and Kliebenstein 2020). Plant secondary compounds restrict the amount of plant tissue lost to herbivores through their negative post-ingestive actions on different cellular and metabolic processes, causing reductions in food intake, digestibility, weight loss and even death (Robbins et al. 1987). Ruminants learn to associate the post-ingestive consequences of eating a specific food with its orosensorial properties (Provenza 1995), and excesses of PSC in foods cause food avoidance because high concentrations of these chemicals cause toxicity; thereby, distancing the animal's physiological processes away from homeostasis (Provenza et al. 2003). In contrast, ruminants form strong preferences for the flavors of food associated to the provision of needed nutrients, approaching the animals' physiological processes towards homeostasis (Villalba and Provenza 1997).

Medicinal and Prophylactic Effects of Plant Secondary Compounds in Forages

The impacts of PSC on herbivores applies to other trophic levels, such as the microorganisms and parasites that inhabit herbivores' bodies and that cause sickness (Lozano 1988). For instance, forage-derived alkaloids, terpenes and phenolics consumed in appropriate doses have antiparasitic and antimicrobial properties (Copani et al. 2013; Hoste et al. 2015; Mueller-Harvey et al. 2009). The same postingestive feedback mechanisms underlying preferences for foods associated to nutrients explains preferences for PSC-containing feeds and forages in infected animals, as ingestion of these medicinal bioactives at appropriate doses also moves the physiology of a sick animal towards a healthy state of homeostasis. In support of this, parasitized lambs showed a greater preference for tannin-containing foods and forages (sainfoin) than non-parasitized animals, and these differences disappeared when parasite loads were eliminated by chemotherapy, suggesting ruminants learn to self-medicate (Juhnke et al. 2012; Villalba et al. 2014).

Besides the direct negative impacts of PSC on parasites and microorganisms (i.e., a medicinal effect), bioactives may provide indirect prophylactic properties to the host through their antioxidant or immunomodulatory properties. For instance, sustained consumption of low doses of plant-derived phenolics, terpenes, flavonoids, and volatile oils have been found to attenuate inflammation and oxidative stress in farm animals, which promote positive effects on performance, health, and product quality (Gessner et al. 2016; Tsiplakou et al. 2021; Nehme et al. 2021). The free radical scavenging activity of some of these chemicals, their metabolic effects such as gene regulation and their antibiotic action, with a contribution to a stable intestinal microbiota and gut health have been proposed as mechanisms underlying the beneficial effects (Gessner et al. 2016; Scott et al. 2022). Continuous ingestion of small daily doses of these bioactives entails a preventive strategy referred to as feedforward or prophylactic self-medication. This process involves routinely ingesting PSC-containing foods with the diet at low daily doses (Vitazkova et al. 2001) in phytochemically-rich forage environments, instead of the active consumption of bioactives through post-ingestive mechanisms described above triggered by endoparasitic infection (i.e., therapeutic self-medication).

The importance of sustained availability of dietary bioactives for reducing oxidative stress (Hao et al. 2020) and inflammation (Jaiswal et al. 2020), and for enhancing immunocompetence (Oh and Histrov, 2016) is becoming evident in ruminant animals. For herbivores, the bulk of any one meal is typically comprised of 3 to 5 plants, but they often eat small amounts of 50 to 75 plants during the day when foraging in diverse plant communities (Provenza 2018). Historically, it has not been recognized that the nutritional and pharmacological properties of these minor components of the diet—best eaten in small doses—enable health. Compared with pastures that lack plant diversity or monotonous feedlot diets, animal welfare and wellbeing—including nutritional, physiological (blood parameters indicative of health), and immunological (immune function) status—all improve when livestock forage on diverse mixtures of phytochemically rich plants (Villalba et al. 2017, 2019; Beck 2020; Beck and Gregorini 2020; Redoy et al. 2020; Nakajima et al. 2021; Garrett et al. 2021ab). This contributes to explain why livestock foraging on phytochemically rich foodscapes require fewer inputs from antiparasitic drugs or antibiotics and they also have low levels of morbidity and mortality compared with animals forced to forage on pastures with few plant species devoid of bioactives or in feedlots (Glasser et al. 2009; Provenza et al. 2019). Moreover, plant diversity in rangelands and pasturelands can increase ecosystem functioning, stability, and services that extend beyond the animal (Isbell et al. 2011; Maestre et al. 2012; Lefcheck et al. 2015).

Bioactives in Forages

The bioactive compounds most often found in grasses are alkaloids, while legumes and non-legume forbs are the source of tannins, isoflavones, and essential oils that have the potential to improve ruminant health or productivity and that may reduce negative impacts on the environment. Unfortunately, the list of forages that readily become established, are productive and persistent, and that tolerate grazing rarely intersects with the list of plant species with the greatest concentrations of beneficial bioactive compounds. Temperate forbs with deep tap roots such as the legumes alfalfa (*Medicago sativa* and *M. sativa* ssp. *falcata*) and sainfoin (*Onobrychis viciifolia*), along with the non-legume forb small burnet (*Sanguisorba minor*), are reliable components of many extensive non-native western rangelands plantings because they are well-adapted to western rangelands and can be managed to persist under grazing. Studies in the Mountain West USA have demonstrated that perennial legumes not only provide relatively high concentrations of protein but accumulate sufficient non-fiber carbohydrates to support ruminant nitrogen retention ranging from 20 to 50% (Stewart et al. 2019; Villalba et al. 2021). Forbs that contain tannins also partition more waste nitrogen into dung than urine, slowing the loss of nitrogen to the environment (Stewart et al., 2019). Perennial forbs and legumes for use as sites of protein and PSC supplementation after rangeland grasses become reproductive were selected in an ongoing study for their retention of nutritive value into late summer and autumn, and for their established value for ruminant grazing (Villalba, 2022). The two-dozen species under study also contain secondary metabolites such as tannins, saponins, terpenoids, and isoflavones. Potential benefits of both primary and secondary nutrients are initially being explored using *in vitro* methodologies to determine effects on rumen methane emissions and dry matter digestion. Small plots in northern, central, and southern Utah will be used to study the rate and reliability of their establishment and their management as components of intensively cultivated protein and PSC supplementation sites.

Impacts of Plant Secondary Compounds on Quality of the Product

Foodscapes with mixtures of grasses, forbs, shrubs, and trees are nutrition centers and pharmacies with vast arrays of phytochemicals which are fundamental for animal health. In turn, human health is linked with the diets of livestock through the chemical features of the plants that livestock eat (Provenza et al. 2015; Gregorini et al. 2017). That includes not only energy, protein, minerals, and vitamins that plants contain, but the tens of thousands PSC plants produce (van Vliet et al. 2020, 2021). This rich pool of compounds is increasingly recognized as responsible—as a complex whole—when trying to understand how plants promote health in herbivores or omnivorous humans who eat plants and meat (Nelson et al. 2017; Barabási et al. 2019). Through their many properties—that include anti-inflammatory, anti-microbial, anti-parasitic, and immunomodulatory effects—phytochemicals bolster health and protect livestock and humans against diseases and pathogens (Tsiplakou et al. 2021; Nehme et al. 2021; Crowe-White et al. 2022).

The benefits to humans of eating phytochemically rich meat may accrue as livestock assimilate some phytochemicals and convert others into metabolites that become muscle and fat, which become health-promoting biochemicals (Provenza et al. 2019; Prache et al. 2020; van Vliet et al. 2021). While phytochemically-rich herbs, spices, vegetables, and fruits (Tapsell et al. 2006), provide a more direct source of phytochemicals, consuming phytochemicals via animal sourced foods is a further avenue to broaden the overall phytochemical richness of human diets, in addition to gaining access to compounds in plants that are toxic for direct human consumption (van Vliet et al. 2021). This expanded pool of phytochemicals and metabolites produced by animals from plants should be considered in attempts to understand benefits to humans, such as damping oxidative stress and inflammation linked with cancer, cardiovascular disease, and metabolic syndrome.

Studies of bison illustrate these points (van Vliet et al. 2022). Compared with bison finished on corn, meadow hay, and alfalfa hay in pens, meat from bison finished on phytochemically rich rangelands has higher amounts of compounds with benefits to bison and human health. Among many others, these include polyphenols, tocopherols, carotene, and omega-3 fatty acids. In contrast, less desirable compounds—such as advanced glycation end-products, triglycerides, and short-chain acyl carnitines—are higher in pen-fed bison. Additionally, the beneficial compounds in pen-fed animals—vitamin B6 and a several phenolics—come from eating meadow hay and alfalfa hay fed as part of their ration as opposed to corn. Bison finished on rangelands also have much improved markers of metabolic health, likely due to the phytochemical richness of their diets and their higher levels of physical activity. To use a human analogy, muscle from range-fed bison is like that of an athlete, while muscle from pen-fed bison is more like that of a human with reduced metabolic health, characterized by enhanced mitochondrial, glucose, and fatty acid metabolism. Bison also suffer less stress when they eat phytochemically rich diets on rangelands as opposed to rations in pens, which further substantiates findings regarding the metabolic health of the bison (van Vliet et al. 2022).

The metabolic effects of eating meat from animals foraging on phytochemically rich diets are partially due to the ability of phytochemicals to curb inflammation (van Vliet et al. 2020). Consuming meat or milk from ruminants raised on non-diverse pastures or grain-finished in feedlots may not have similar beneficial effects on inflammation (Arya et al. 2010; Sofi et al. 2010; Gilmore et al. 2011. Low-grade systemic inflammation, characterized by elevated levels of cytokines (e.g., interleukin-6, tumor necrosis factor-alpha, and C-reactive protein), contributes to metabolic disease, type II diabetes, heart disease, cancer, and arthritis (Libby 2007). Notably, cytokines respond within a meal (Holmer-Jensen et al. 2011), with increasing likelihood of developing diseases when meals that generate an exaggerated inflammatory response become dietary habits (Esposito and Giugliano 2006). Moderating inflammation through wholesome diets can prevent or treat metabolic disease.

Restructuring of Rangelands and Pasturelands with Bioactive-Containing Forages

Restoration "islands" or plant patches are being used as a novel strategy to rehabilitate degraded and monotonous habitats efficiently and effectively in neotropical forests and some grassland ecosystems (Shaw et al. 2020). A fundamental premise is that these islands become sources of propagules that disperse outward across the degraded landscape, facilitating recovery (Reis et al. 2010). These islands can be viewed as supplementation patches where legumes forbs and shrubs could be established in the landscape, providing nutrients and bioactives to enhance animal productivity and health through the aforementioned process of self-medication and feedforward mechanisms. Beyond being a significant source of nutrients and bioactives to livestock, islands of bioactive-containing forages can serve as refugia and corridors within monotonous landscapes by providing habitat (e.g., structural cover, insect populations), connectivity and resources for target plant and animal species (Fischer et al. 2014) that produce multi-functional working landscapes (McGranahan 2014). Transdisciplinary collaborations between, for example, agronomists, landscape architects, range scientists, nutritionists, and land managers could lead to integrated approaches (e.g., When, where, which species and combinations to use) within the landscape that transform landscapes into more sustainable, resilient and biodiverse systems.

Conclusions

Emerging data from the fields of rangeland sciences, animal science, and human nutrition indicate that increasing availability of bioactive-containing forages in rangelands and pasturelands has the potential to improve animal health and the nutraceutical properties of meat and milk. Single forage species limit the ability of grazers to improve their health prophylactically and medicinally and consequently constrain the healthfulness of meat and milk products. Thus, through strategic distribution across space and time of phytochemically-rich forages in rangelands and pasturelands, there is tremendous potential to synergistically complement and provide new dimensions (prophylactic-medicinal, product quality) to forages available to animals. Promoting plant diversity also provides broader ecosystems services, potentially improving health along the plant-animal-human health continuum.

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