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Plant secondary compounds in Mediterranean shrubs: Phytotoxins or medicines

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Abstract. Plant secondary metabolites (also called phytotoxins; natural products) are molecules existing in most vascular plants that are not necessary for their survival, but in higher concentrations they protect plants from consumers or from pathogens. These phytochemicals can adversely affect cellular and metabolic processes in herbivores, but also at low doses and in appropriate mixtures, they can have beneficial effects on animal nutrition, health and other therapeutic impacts. In this paper, we demonstrate the potential effects of plants with medicinal properties on animal foraging behavior as a function of the consequences they experience after ingestion of Mediterranean shrubs that are rich in phytotoxins. This mechanism –behavior by consequences– suggests animals are able to meet nutritional requirements and self-select certain plants with medicinal properties if they are offered the opportunity to do so when foraging in diverse Mediterranean shrub communities. Understanding the feeding behavior of ruminants when offered a variety of plant species is necessary to be able to improve their health and well-being by reducing levels of stress and fear; it may also lead to the early detection of illness. Thus, management strategies in biochemically/biologically diverse ecosystems should benefit from allowing ruminants to manifest their feeding preferences.

Keywords. Mediterranean shrubs – Herbivores – Secondary compounds – Medicinal plants – Phytotoxins.

Composés secondaires végétaux dans les arbustes méditerranéens : phytotoxines ou médicaments

***Résume**. Les métabolites secondaires de plantes (également appelés phytotoxines; produits naturels) sont des molécules fabriquées dans la plupart des plantes vasculaires qui ne sont pas nécessaires à leur survie, mais qui, à des concentrations plus élevées, les protègent des consommateurs ou des agents pathogènes. Ces composés phytochimiques peuvent avoir des effets néfastes sur les processus cellulaires et métaboliques chez les herbivores, mais aussi à faibles doses et dans des mélanges appropriés, ils peuvent avoir des effets bénéfiques sur la nutrition, la santé et d'autres effets thérapeutiques des animaux. Dans cet article, nous démontrons les effets potentiels de plantes ayant des propriétés médicinales sur le comportement alimentaire des animaux en fonction des conséquences qu'elles subissent après l'ingestion d'arbustes méditerranéens riches en phytotoxines. Ce mécanisme –comportement par conséquences– suggère que les animaux sont capables de satisfaire les besoins nutritionnels et de sélectionner eux-mêmes certaines plantes aux propriétés médicinales si l'on leur en donne la possibilité lorsqu'elles cherchent de la nourriture dans diverses communautés arbustives méditerranéennes. Comprendre le comportement alimentaire des ruminants lorsqu'on leur propose une variété d'espèces végétales est nécessaire pour pouvoir améliorer leur santé et leur bien-être en réduisant les niveaux de stress et de peur. Cela peut également conduire à la détection précoce de la maladie. Ainsi, les stratégies de gestion dans des écosystèmes diversifiés biochimiquement/biologiquement devraient permettre aux ruminants de manifester leurs préférences en matière d'alimentation.*

***Mots-clés**. Arbustes méditerranéens – Herbivores – Composés secondaires – Additifs alimentaires – Plantes médicinales – Phytotoxines.*

I – Introduction

Ruminants foraging on Mediterranean rangelands encounter plant species that differ in their flavor and nutrient concentrations. Plants also contain secondary compounds that at excessive doses in plants can adversely affect herbivores through their negative actions on cellular and metabolic processes (Cheeke, 1998), but at the appropriate doses many of these phytotoxins may have medicinal benefits. The influence of plant secondary compounds on diet selection of mammalian herbivores is recognized (Mc Arthur *et al.,* 1991; Mc Arthur *et al.,* 1993; Duncan *et al*., 1994), and it is known that interspecific differences exist among ruminants for tolerance and response to phytochemical defenses. However, interspecific differences in diet selection in response to phytochemical compounds have received little consideration as a basic factor influencing diet selection of herbivores. In plant communities with a diversity of plants species, animals may consume a variety of foods, and thus they can potentially benefit from secondary compounds in their diet. At appropriate doses, secondary compounds can benefit ruminants through suppression of bacteria, parasites, and fungi that inhabit herbivores bodies and cause impairment of herbivore health (Engel, 2002). The nature of this dual action (i.e., toxin/medicine) is merely a matter of dosage and a consequence of the animals tolerance and current physiological state (Plotkin, 2000). Secondary compounds are increasingly recognized as important in animal health and nutrition, though historically they were thought by agriculturalists and ecologists alike to adversely affect herbivores (Dawson *et al*., 1999). In this paper, we discover emerging information on how secondary compounds in plants with medical properties may directly and/or indirectly help prevent and eliminate different diseases in livestock. We explore how health benefits may be enhanced by understanding the interplay between plant secondary compounds and foraging behavior.

II – Materials and methods

Three herbs with medicinal properties [*Foeniculum vulgare* Mill. (Apiaceae), *Matricaria chamomilla* L. (Asteraceae) and *Achillea millefolium* L. (Asteraceae)] were examined to determine their influence on intake of high-terpene shrubs (*Juniperus phoenicea* L.), one of the most abundant shrub species in Mediterranean maquis plant communities. *Juniperus phoenicea* was fed to goats either with (treatment) or without (control) access to the three above-mentioned herbs with medical properties (fennel, chamomile and yarrow).

The experimental animals (n = 12; mean weight ± SEM = 12.6 ± 1.1 kg) were 4-month-old goats (a mixture of domestic breed crossed with Saanen and Alpine breeds). All experimental animals were raised on the same shrublands and were experienced in grazing on Mediterranean maquis vegetation. Prior to the experiment animals went through a 5-day pre-conditioning period by adding 200 g of barley mixed with 100 g of every shrub used in experiments. Animals were divided into two groups of six animals (control and treatment). In the first set of research, the three separate experiments were conducted, wherein the animals were offered the various diets daily in a 10 day period. At 8:00, in all experiments animals from both groups were fed with 200 g of barley. Shrub leaves and current season's growth (i.e., twigs) were clipped and ground to 1 cm length with a chipper, mixed for uniformity, placed in woven, polyethylene feed sacks, and stored at 4ºC. In the first experiment, we compared intake of *Juniperus phoenicea* alone (control group) with intake of *J. phoenicea* and *Achillea millefolium* (treatment group) offered at the same time in separated feed boxes. Animals in both groups (control and treatment) were offered 200 g of J. *phoenicea* in food boxes from 09:00 to 14:00 h. Animals and food boxes were checked every 30 min and additional J. *phoenicea* biomass was added as needed. Animals in the treatment group also received 200 g *A. millefolium*, divided in four 50 g meals offered at 9:00, 10:15, 11:30, and 12:45 h. The same protocol was used in the following experiments. In the second experiment, the animals in the treatment group were offered *J. phoenicea* and *M. chamomilla*, while control animals were only fed with

J. phoenicea. In the third experiment, the control group of goats was offered *J. phoenicea* alone, while treatment group of goats was fed a *J. phoenicea* and *F. vulgare.* The second experiment was conducted on the same manner as the first one, including 15 days rest for animals and precondition period. In each of the 10-day experiments, goats were offered juniper biomass ad libitum.

In the second set of research, the four consecutive experiments the phylogenetical similar shrubs of the genius *Quercus* offered to the goats in the first experimental group, while the phylogenetical diverse Mediterranean shrubs offered to the goats in the second experimental group. Shrubs were harvested each week from the vicinity of the feeding experiments. Every day before the experiment, sufficient feed was removed from cold storage and offered to the animals. In all experiments both groups of animals were supplemented with barley (200g) at 08:00 hours, then offered the ground shrubs from 08:30 to 14:00 hours. Shrubs were fed in individual boxes to each animal, and the amounts replenished as necessary during the day. Any uneaten amounts were weighed. Trials lasted for 10 days and ran consecutively. Goats in the *Quercus*-group were fed different species of oak (*Quercus*) genus. Goats in the diverse genera-group were fed species that belong to different genera, families, order and subclasses. From the phylogenetic point of view the shrubs species offered to goats in the second group are very heterogeneous and much more phytochemical diverse.

The experimental design for the shrubs fed individually to goats was a completely random design with a separate analysis for each shrub in both experiments. The model included two treatments per experiment, with individual animals nested within treatments, and repeated measures over the 10-days. The total daily amount consumed of each shrub offered was used as the dependent variable in the analysis. Analyses were conducted using the MIXED procedure of SAS (SAS Inst. Inc., Cary, NC; Version 9.1 for Windows). All analyses on shrub intake were adjusted for body weight prior to the analysis (g/kg BW).

III – Results and discussion

Average daily intake was much greater when fennel, chamomile and yarrow were included in combination with rich-terpene shrub *Juniperus phoenicea* (Fig. 1). Rather than substituting the more palatable fennel for shrubs, animals continued to eat about the same amount of shrubs biomass while increasing total intake. Thus, fennel holds promise as a supplemental feed for ruminants consuming shrubs with high concentrations of terpenes. What is not known is whether fennel, chamomile and yarrow can ameliorate effects of secondary compounds consumed by livestock and whether their effects are altered by the biochemical complexity of shrubs consumed.

When goats were fed with different Mediterranean shrubs that belong to different species and genera, they ate more foliage than goats fed with different combinations of high-tannin shrubs that belong to different species of the same *Quercus* genus (*Q. pubescens, Q. ilex, Q. cerris and Q. petraea*) (Fig. 2). Based on the higher biological/biochemical diversity of shrubs, goats increased their intake of the phylogenetically more distant shrubs when compared to more related Mediterranean oak species regardless of their nutritional value. These results support hypothesis that goats ate more of the biochemically diverse shrubs than the biochemically similar oak species. Given a choice of two genetically more diverse and more similar shrubs categories offered to goats, we expected a higher preference for biochemically diverse shrubs and these differences increased from the second to the last experiment.

Mediterranean shrubs produce a variety of secondary metabolites that are toxic and deterrent to herbivores (Silanikove *et al*., 1996). These substances are usually assumed to serve as chemical defenses against herbivores in those ecosystems (Rogosic *et al*., 2007), but at appropriate doses can suppress production of the pathogens that can impair herbivore health (Engel, 2002). The difference between a toxin and a medicine is merely a matter of dosage (Plotkin, 2000). Still, we know very

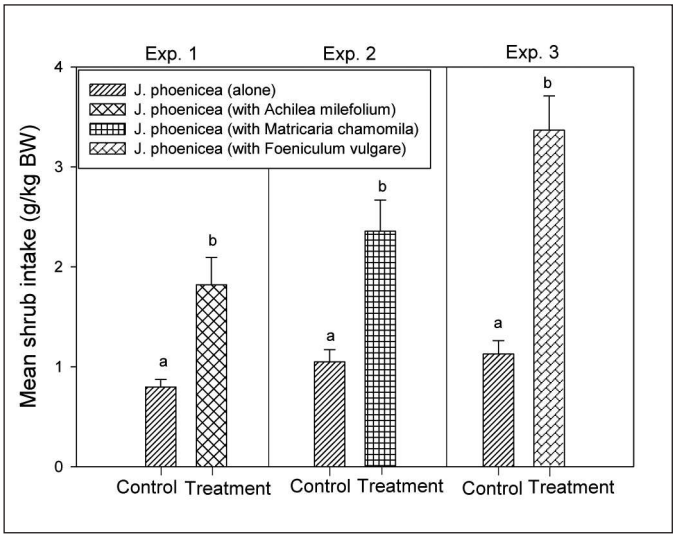

Fig. 1. Intake (g/kg BW) of goats fed different combinations of high-terpene shrub *Juniperus phoenicea* and herbs *Foeniculum vulgare, Matricaria chamomilla* and *Achillea millefolium* with medical properties; n = 6 per treatment group; (*P* < 0.01).

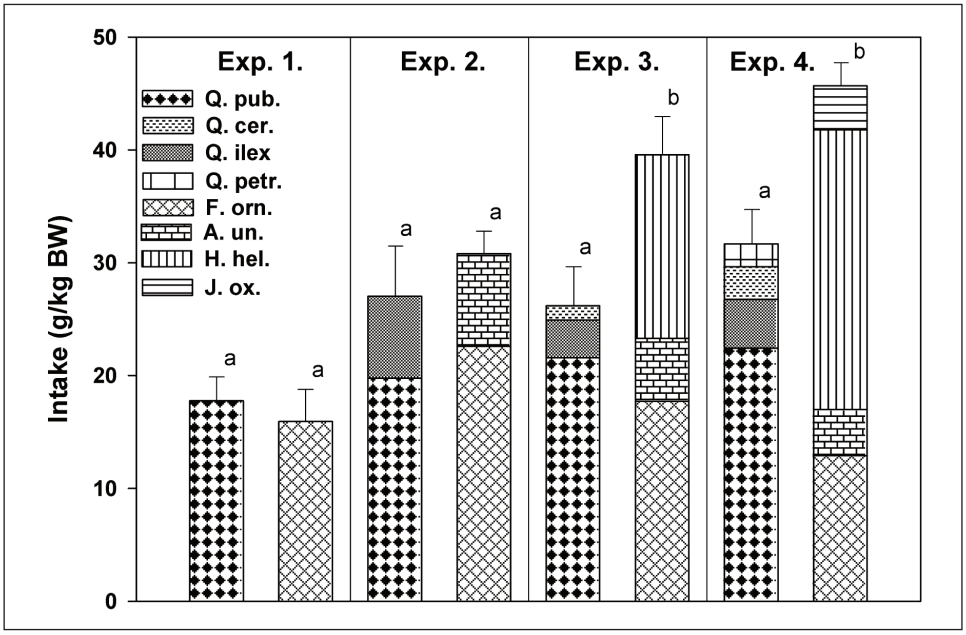

Fig. 2. Total shrubs intake (g/kg BW ± SE) of goats fed different combinations of high-tannin shrubs in group 1 that belong different species of the same *Quercus* genus (*Q. pubescens, Q. ilex, Q. cerris and Q. petraea)* and shrubs in group 2 that belong to different species and different genus (*Fraxinus ornus*, *Arbutus unedo*, *Hedera helix* and *Juniperus oxycedrus*) n = 6 per treatment group; P < 0.01.

little about how herbivores might learn to use secondary compounds for health and medicinal benefits. While much remains to be learned, herbivores can learn to use medicines to attenuate the aversive effects of acidosis as well as tannin and terpene toxicosis (Provenza and Villalba, 2006). They also select diets that (i) provide necessary amounts of energy and protein, (ii) synchronize the supply of energy and protein, (iii) balance supplies of macronutrients and toxins, and (iv) benefit different kinds of complementary toxins (Rogosic *et al*., 2003; 2006). Above mentioned examples show that herbivores differ the main properties and interactions among nutrients, toxins, and medicines.

The relationship between phylogenetic distances implies a greater diversity in plant secondary compounds, and is a key to understanding mechanisms of plant animal interactions in Mediterranean shrubby ecosystems. Secondary metabolites function as a defense against herbivores, so their class, concentrations and diversity determine herbivore preference (Rogosic *et al*., 2007), and therefore have an important role in the plant's survival in natural conditions. Likewise, they represent adaptive characteristics that have been subjected to natural selection during evolution (Rasmann and Anurag, 2011).

IV – Conclusions

According to the results achieved in the experiments presented, natural plant communities like Mediterranean rangelands with diverse mixtures of plant species are literally nutrition centers and pharmacies with vast arrays of primary (nutrient) and secondary (pharmaceutical) compounds vital in the nutrition and health of plants and herbivores. Self-medication has the potential to facilitate the design of sustainable grazing systems to improve the quality of land as well as the health and welfare of animals. Understanding foraging as the dynamic quest to achieve homeostasis will lead to implementing management programs where herbivores have access not only to diverse and nutritious foods but also to arrays of medicinal plants.

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