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Can animals use foraging behaviour to combat parasites?

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Host–parasite interactions are often seen as an arms race, with parasites attempting to overcome host resistance to infection. Herbivory is a common route of transmission of parasites that represents the most pervasive challenge to mammalian growth and reproduction. The present paper reviews the foraging skills of mammalian herbivores in relation to their ability to exploit plant properties to combat parasites. The starting point is that foraging behaviour may ameliorate the impact of parasitism in three ways; hosts could: (1) avoid foraging in areas contaminated with parasites; (2) select diets which increase their resistance to parasites; (3) select for foods containing anti-parasitic properties (self-medication). Details are given of the pre-requisite skills needed by herbivores if they are to combat parasitism via behaviour, i.e. herbivores are able to: (a) determine their parasitic state and alter their behaviour in relation to that state (behaviours 1, 2 and 3); (b) determine the environmental distribution of parasites (behaviour 1); (c) distinguish plant species or plant parts that increase their resistance to parasites (behaviour 2) or have anti-parasitic properties (behaviour 3). Mammalian herbivores cannot detect the presence of the parasites themselves and must rely on cues such as faeces. Despite the use of these cues contacting parasites may be inevitable and so mechanisms to combat parasitism are necessary. Mammalian herbivores have the foraging skills needed to exploit the heterogeneous distributions of nutrients and parasites in complex foraging environments in order to avoid, and increase their resistance to, parasites. Current evidence for the use of plant secondary metabolites (PSM) by herbivores for self-medication purposes remains equivocal. PSM have both positive (anti-parasitic) and negative (toxic) effects on herbivores. Here details are given of an experimental approach using tri-trophic (plant–herbivore–parasite) interactions that could be used to demonstrate self-medication in animals. There is strong evidence suggesting that herbivore hosts have developed the foraging skills needed to take advantage of plant properties to combat parasites and thus use behaviour as a weapon in the host–parasite arms race.

Acquired immunity: Grazing behaviour: Parasite control: Parasite distribution: Self-medication

‘Krauter und Wurzeln findet ein jeder sich selbst, wir lernten’s im Walde vom Tier (Herbs and roots each of us finds for himself. From beasts of the forest we learned).

Parsifal; R. Wagner

The arms race between parasites and their hosts is well documented, with parasites attempting to overcome host resistance to infection. There is often a fine balance between the ability of parasites to persist in host populations and the ability of hosts to control parasitism in both natural and agri-

cultural systems (Grenfell & Dobson, 1995). The common expectation is that parasites should persist, given their generally greater rate of reproduction and thus ability to adapt or evolve and stay one step ahead of a host’s ability to control parasites (Grenfell & Dobson, 1995). Parasitism

Abbreviations: CT, condensed tannins; PSM, plant secondary metabolites.

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often represents the most pervasive challenge to host survival and reproduction, and thus it might also be expected that a considerable evolutionary pressure exists on hosts to evolve mechanisms and behaviours to counter these effects (Hart, 1990). The present paper reviews the behaviours that hosts have developed to cope with parasites. Host interactions with parasites often occur in foraging environments, and foraging behaviour may be used to combat parasites in three ways (from Lozano, 1991). Hosts could:

- behaviour 1, avoid foraging in areas that are contaminated by parasites (i.e. prevent parasitism);
- behaviour 2, select diets that increase their resistance to parasites;
- behaviour 3, select for foods containing anti-parasitic properties.

Herbivory is a common route of parasite transmission, and in the present review the literature on mammalian herbivore–gastrointestinal parasite interactions has been extensively drawn on to support the concept of animal hosts using the three behaviours to exploit plant properties to combat and avoid parasites. The term ‘plant properties’ includes their internal properties (e.g. nutrient concentration in the tissues) and external properties (e.g. faecal contamination of the plant structure).

Here consideration is given to how animals use foraging behaviour to combat parasites in both simple and complex environments. In simple environments animals may be seen as facing straightforward choices, e.g. in the case of behaviour 1 a choice between a parasite-contaminated and a parasite-free forage patch. Many species of gastrointestinal parasites of mammalian herbivores are deposited in the environment in faeces and transmitted via grazing (Sykes, 1987). As a consequence the vegetation around faeces is frequently contaminated with infective-stage parasite larvae (Sykes, 1987). All else being equal, this heterogeneous distribution of parasites in the environment creates an opportunity for hosts to avoid parasite-contaminated areas (i.e. behaviour, 1).

In more complex environments animals may not face such straightforward choices. For example, faeces not only contain parasites, but also nutrients that leach into the surrounding soil creating a sward patch that is relatively nutrient (e.g. N) rich. Thus, the deposition of nutrients and parasites via faeces may create a grazing environment in which the distributions of parasites and nutrients coincide. As a consequence, grazing herbivores may face a trade-off between the costs of parasite ingestion and the benefits of increased nutrient intake, both the result of faecal contamination of swards. As mammalian resistance to gastrointestinal parasitism can be influenced by nutrition (see p. 363) in the presence of a nutrition *v.* parasitism trade-off, there may be a conflict between carrying out behaviours 1 and 2.

The grazing decisions of herbivores in relation to the heterogeneous distributions of parasites and nutrients in simple and complex grazing environments will determine their intake of both parasites and nutrients, and thus their fitness and survival. Such decisions are central to our understanding of the ability of animals to use behaviour to combat parasites. Here the evidence that herbivores have

the ability to employ behaviours 1, 2 and 3 to ameliorate the consequences of parasitism is reviewed. First, details are given of how herbivores can avoid parasites and select diets to increase resistance to parasites in simple grazing environments. Then, the way in which the trade-off theory can be used to interpret herbivore foraging decisions in complex environments, and specifically when faced with nutrition *v.* parasitism trade-offs, is demonstrated. Finally, a description is given of how certain plants have negative effects on both herbivore hosts and their parasites, creating a naturally-occurring trade-off, with details of how the occurrence of this trade-off could be used to experimentally demonstrate self-medication by animals.

Can herbivores determine and thus avoid parasite-infested foods (behaviour 1)?

It is perhaps not surprising that where animals can detect parasites in the environment they avoid them, e.g. mammalian hosts avoid ectoparasite-infested environments (Folstad *et al.* 1991; Richner, 1998; Engel, 2002). However, hosts may not be able to directly detect their parasites in the environment. The populations of many species of gastrointestinal helminth parasites, deposited in the environment in faeces, are concentrated in swards around faeces. In grazing systems mammalian herbivores cannot detect infective-stage gastrointestinal nematode parasites on swards and thus must rely on the presence of faeces as a cue to the presence of parasites (Cooper *et al.* 2000). The aggregation of faeces may itself be a mechanism used by hosts to concentrate their parasites at particular sites, e.g. red howling monkeys (*Alouatta seniculus*) select non-feeding sites for the deposition of faeces and thus parasites (Gilbert, 1997). The observed heterogeneous distributions of faeces, and thus parasites, that are often concentrated at latrines and/or campsites in the environment may thus reflect parasite-avoidance strategies of mammalian hosts. It has been demonstrated that in simple environments (i.e. where herbivores are faced with a choice between faeces-contaminated and non-contaminated swards) herbivores avoid grazing swards contaminated with faeces, and thus parasites, in agricultural (Bao *et al.* 1998; Hutchings *et al.* 1998; Cooper *et al.* 2000) and natural systems (van der Wal *et al.* 2000; Hutchings *et al.* 2002b). All else being equal, foraging animals not only avoid swards contaminated with faeces from their own species (Bao *et al.* 1998; Hutchings *et al.* 1998; Gilbert, 1997), but also swards contaminated with the faeces of other species, when they have the option of selecting non-contaminated forage (e.g. Hutchings & Harris, 1997).

For herbivores in grazing environments where forage may become limiting (e.g. agricultural fields) the area of clean pasture will decline with time (Haynes & Williams, 1993). This situation is due to animals selectively grazing and further contaminating the non-contaminated pasture, leaving them to make grazing decisions based on the age and/or amount of faecal contamination (i.e. being forced to graze faeces-contaminated pasture; Hutchings *et al.* 1998). In this instance behavioural strategies to reduce the intake of parasites whilst maintaining an adequate nutrient intake would be advantageous (Hart, 1990). If forced to graze faeces-contaminated swards (i.e. only contaminated sward

is available) mammalian herbivores graze the upper portion of the sward, acting to reduce further parasite intake since the vast majority of parasites persist in the lower portions of the sward (Familton & McAnulty, 1997; Hutchings *et al.* 1998). However, as the upper portion of the sward contains the highest levels of N (Haynes & Williams, 1993), it also results in animals consuming the most nutritious portion of the sward (Hutchings *et al.* 1999).

These faeces-avoidance, and thus parasite-avoidance, behaviours are seen in non-parasitised animals, but are markedly exaggerated in parasitised animals; i.e. relative to non-parasitised animals, parasitised animals show increased avoidance of contaminated swards and when grazing contaminated swards they graze further from the soil surface. This exaggeration of faeces-avoidance behaviours results in parasitised animals almost completely avoiding the contaminated swards, and if there is no choice they graze only the very tops of contaminated swards in order to minimise their parasite intake (Hutchings *et al.* 1998, 1999). The cost of gastrointestinal parasitism to mammalian herbivores is an increased endogenous loss of N through damage to gastrointestinal tissue (Poppi *et al.* 1986; Bown *et al.* 1991). The exaggeration of parasite-avoidance behaviours in parasitised animals compared with non-parasitised animals could be attributed to the increased risk of mortality from further parasite intake (Coop *et al.* 1982; Fox, 1997; Lochmiller & Deerenberg, 2000).

However, relying on cues to determine the distribution of parasites in the environment has its limitations. Comparisons of bacterial *v.* nematode parasite transmission from faeces-contaminated swards to grazing herbivores highlight such limitations. If animals use faeces as a cue to the presence of parasites the decomposition of the faeces over time could result in a reduction in the strength of the cue (Hutchings *et al.* 1998). As a consequence, herbivores avoid fresh faeces most strongly and this aversion declines with time. Bacterial pathogens such as *Mycobacterium bovis* cannot multiply once deposited in the environment and are killed by weathering (e.g. radiation from the sun); thus, their numbers decline with time (King *et al.* 1999). The strong avoidance of fresh faeces would thus result in herbivore hosts avoiding the highest concentrations of bacterial parasites in faeces. However, for nematode parasites (e.g. gastrointestinal worms) it often takes a number of weeks for the parasite eggs in the faeces to develop into infective-stage larvae that migrate within the sward (Familton & McAnulty, 1997). For example, the eggs of *Ostertagia circumcincta*, a gastrointestinal nematode worm of sheep, take approximately 3 weeks to develop into infective-stage larvae when they migrate from the faeces onto the surrounding sward, thereby representing a risk of infection to grazing herbivores (Familton & McAnulty, 1997). The reduction in avoidance of faeces with time can lead to a paradox, in that older faeces are avoided to a lesser extent but represent a greater risk of parasitism than fresh faeces that are most strongly avoided but represent little risk from parasitism (Hutchings *et al.* 1998). The avoidance of faeces *per se*, and thus the parasites therein, has obvious evolutionary advantages. However, having to resort to using cues to the presence of parasites may limit a host's ability to completely avoid parasites.

Also, animals in sward-depleted environments may not have a choice and may be forced to graze faeces-contaminated, and thus parasite-contaminated, swards. Given these difficulties in completely avoiding parasites in foraging environments, contacting parasites may be inevitable, and so animals also need behaviours to combat parasites.

Can parasitised hosts select diets that increase their resistance to parasites (behaviour 2)?

Parasitised animals often rely on their acquired immune system to resist parasitic infection. There are two phases of the acquired immune response: acquisition of immunity, when the host recognises the presence of parasite invasion of its tissues; expression of immunity, when the host mobilises its cellular and humoral responses to combat the infection. The up-regulation of the immune system to combat a parasitic infection may have considerable nutrient costs (Sheldon & Verhulst, 1996; Goosens *et al.* 1997; Coop & Kyriazakis, 1999, 2001; Lochmiller & Deerenberg, 2000). To address the question, can animals use diet selection to increase their resistance to parasites, it must be established that diet can influence immunity. The effects of diet during the acquisition of immunity are thought to be limited (Abbott *et al.* 1988; Bown *et al.* 1991; Coop *et al.* 1995; van Houtert *et al.* 1995; Kyriazakis *et al.* 1996; Kahn *et al.* 2000). Thus, the answer to the question, can diet selection be used to increase rates of acquisition of immunity in parasitised animals, is no, as there are probably limited nutrient costs associated with the phase of acquisition of immunity (Coop & Kyriazakis, 1999, 2001). The main influence of dietary supplementation of parasitised animals is on the extent of expression of immunity, and this effect has been widely demonstrated (Abbott *et al.* 1988; Bown *et al.* 1991; Mansour *et al.* 1991; Kambara *et al.* 1993; Coop *et al.* 1995; van Houtert *et al.* 1995; Datta *et al.* 1998; Houdijk *et al.* 2000, 2001). There is, therefore, the potential for diet selection to be used by hosts to substantially increase their resistance to parasitism.

The concept of nutritional wisdom, where animals select diets in relation to their specific nutrient requirements, is well studied. For example, parasitised animals select protein-rich diets that may help to counter the losses through parasitism and increase their resistance to parasitism (Kyriazakis *et al.* 1994, 1996). It is only relatively recently that information has become available on the extrapolation of the findings of Kyriazakis *et al.* (1996) to grazing systems where herbivores have access to plant communities. Sheep with subclinical gastrointestinal parasitism have been shown to select a diet higher in relatively-N-rich clover (*Trifolium* spp.) than non-parasitised sheep, when given access to grass-clover swards (Cosgrove & Niezen, 2000; Hutchings *et al.* 2000a). However, whether the change in diet selection recorded as a response to parasitism (i.e. the selection for N-rich diets in the experiments described earlier) is enough to markedly increase host resistance to parasitism is unknown. Until demonstrated, some scepticism about the ability of parasitised animals to actively employ behaviour 2 to combat their parasites is likely to remain.

Implementing behaviours 1 and 2 in complex environments

The behavioural rules used by foraging animals in simple environments seem straightforward; where possible avoid parasites (behaviour 1) and select nutrient-rich forage to resist parasitism (behaviour 2). However, this solution may not be applicable in more complex environments where animals face a dilemma in that selection for nutrient-rich forage may also lead to increased parasite intake. For example, as a consequence of the concentrating effect of digestion and defecation there tend to be higher levels of nutrients such as N in the tissues of plants in areas associated with faecal deposits in grazing environments (Haynes & Williams, 1993). N content is positively associated with sward darkness, and mammalian herbivores use sward darkness as a cue when selecting N-rich swards (Bazely & Ensor, 1989; Bazely, 1990). Also, the initial avoidance of faeces-contaminated swards by herbivores results in faeces being associated with relatively tall swards, offering a greater potential forage intake rate to grazing herbivores (Hutchings *et al.* 2001a). Sward height is a powerful cue used by mammalian herbivores to select for increased forage intake rate (Black & Kenney, 1984). As such, tall dark swards associated with faeces may be attractive to grazing herbivores. The heterogeneous distributions of faeces (and thus parasites) and sward structure are seen visually in grazing systems as a patchwork of tussocks (patches of relatively tall nutrient-rich and faeces-contaminated sward) surrounded by gap swards (short non-contaminated sward; Hutchings *et al.* 2002a,b). A foraging herbivore may be faced, therefore, with a trade-off between nutrient ingestion (nutrient richness and intake rate) and parasite avoidance, and thus conflict between the application of the parasite-avoidance and nutrient-ingestion strategies (behaviours 1 and 2). Such nutrition *v.* parasitism trade-offs are not limited to mammalian herbivore systems. Oystercatchers (*Haematopus ostralegus*) feeding on cockles (*Cerastoderma edule*) infected with helminth parasites represent another example of where a foraging animal may face a nutrition *v.* parasitism trade-off (Norris, 1999), since level of parasite infection increases with cockle size. To maximise energy intake rate birds should select the larger cockles, but to minimise intake rate of parasites birds should select small cockles. The selection of intermediate-sized cockles by oystercatchers suggests that they may make compromises (i.e. trade-offs) between the conflicting intakes of nutrients and parasites (Norris, 1999). A further recently reported example of a nutrition *v.* parasitism trade-off in a foraging animal is the tadpole of the spadefoot toad (*Spea bombifrons*) feeding on bacteria-infected prey species (Pfenning, 2000). Prey species that represent the greatest nutrient benefit also represent the greatest risk of parasitism to the tadpoles. Nutrition *v.* parasitism trade-offs occur in a wide range of natural systems, and the decisions of animals in relation to such trade-offs may determine their intake of nutrients and parasites, and thus fitness and survival.

Given the occurrence of complex nutrition *v.* parasitism trade-offs in natural and agricultural systems, trade-off theory may help interpret animal foraging decisions (i.e. foraging decisions can be seen as having costs and benefits

to the animal). The use of the trade-off theory to interpret animal behaviour is not new. In terms of animal foraging behaviour and nutrition the trade-off theory has previously been used with great effect to interpret the behaviour of animals facing foraging–predation-risk trade-offs, e.g. situations in which the most nutrient-rich patches in an environment also represent the greatest risk from predation (Lankford *et al.* 2001; Walther & Gosler, 2001; Grand, 2002; van der Veen, 2002). The trade-off theory has also often been used to interpret the optimal foraging decisions of animals (for two of the most recently reported examples, see Basset *et al.* 2002; Hassall *et al.* 2002) and the parental investment of animals facing trade-offs between current and future reproduction (Tatar & Carey, 1995; Wright *et al.* 1998; Courchamp *et al.* 2002; Tveraa & Christensen, 2002; Webb *et al.* 2002).

When faced with a nutrition *v.* parasitism foraging trade-off an animal might be expected to select a diet that maximises the nutritional benefits whilst minimising the parasitic costs, i.e. solve the trade-off (Sweitzer, 1996; Wright *et al.* 1998; Lewis *et al.* 2001). In grazing systems the trade-off poses a dilemma to an animal as to which behaviour to adopt: (1) to select for the nutritional advantage to enhance their immune function, but at the same time accepting greater parasite intake; (2) to increase their avoidance of faeces and thus parasites, but at the same time accepting a lower forage intake rate from the shorter swards. The solution to this dilemma is not straightforward, since a number of environmental and animal factors might be expected to affect the relative costs and benefits of the trade-off.

There is a growing body of evidence suggesting that host foraging behaviour can be influenced by their physiological state (Parsons *et al.* 1994; Penning *et al.* 1995; Gibb *et al.* 1999; Ingrand *et al.* 2000) and specifically their parasitic or immune state (Barnard & Behnke, 1990; Sheldon & Verhulst, 1996; Coop & Kyriazakis, 1999, 2001; Lochmiller & Deerenberg, 2000; Norris & Evans, 2000; Zera & Harshman, 2001). In relation to a host's physiological state, animal grazing decisions might be affected by states that affect the relative costs and benefits of the trade-off, e.g. their ability to combat parasitism (e.g. their immune or parasitic state) and their drive to consume nutrients (e.g. their feeding motivation). In relation to immune status, Fig. 1 shows that when faced with a nutrition *v.* parasitism trade-off the behaviour of parasite-naïve and parasite-immune herbivores (sheep) can be markedly different, despite them both having little or no parasite burden (Hutchings *et al.* 1999). Thus, parasite-naïve animals, being at greater risk from parasite ingestion than parasite-immune animals, are more averse to faeces-contaminated swards even if they do offer a nutrient advantage (Hutchings *et al.* 1999). This finding suggests that hosts have mechanisms that enable them to determine their immune state, and that this ability is not necessarily dependent on the presence of parasites. This relationship between behaviour and the immune state is consistent with the concept of a communication axis between the brain and the immune system (Tomaszewska & Przekop, 1997; Dantzer *et al.* 2000; Elenkov *et al.* 2000). In relation to parasite burden, the grazing decisions of sheep at the same stage of immunity to

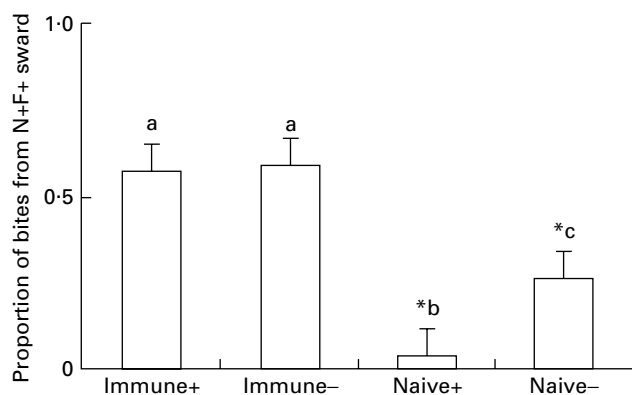


Fig. 1. Effect of parasitic state on sheep grazing decisions. Proportion of bites taken from a nitrogen-rich (N+) faeces-contaminated (F+) sward when paired with a nitrogen-poor non-contaminated sward. Immune, animals immune to *Osertagia circumcincta*; naive, parasite-naive animals; +, -, the presence and absence of a parasite burden respectively. Values are back transformed means and upper 95 % CI represented by vertical bars. ^{a,b,c} Mean values with unlike superscript letters were significantly different ($P < 0.05$). Mean values were significantly different from those for random sward selection (i.e. 0.5): * $P < 0.05$. (From Hutchings *et al.* 1999.)

gastrointestinal parasites can be affected by parasite burden (Hutchings *et al.* 2002a). Sheep with a higher parasite burden avoided parasite-rich swards (offering a nutrient advantage) to a greater extent than sheep with a lower parasite burden (Hutchings *et al.* 2002a). This finding suggests that an animal is 'aware' of the presence and the size of the parasite population it hosts. In addition, the feeding motivation of a parasitised herbivore has been shown to have dramatic effects on sward selection when faced with a nutrition *v.* parasitism trade-off (Hutchings *et al.* 2001b). For example, a strong aversion to tall faeces-contaminated swards (i.e. offering greater nutrient intake rate) in favour of short non-contaminated swards by parasitised animals was overcome by increased feeding motivation (Hutchings *et al.* 2001b).

The costs and benefits of the nutrition *v.* parasitism trade-off in grazing systems are not only affected by the physiological state of the animals, but also by sward characteristics. In terms of sward characteristics the selection for N-rich swards (dark swards) by herbivores cannot completely overcome faeces, and thus parasite, avoidance even in parasite-immune animals, as they do not markedly select faeces-contaminated N-rich swards (Fig. 1; Hutchings *et al.* 1999, 2000b). However, the selection for tall vegetative swards offering greater nutrient intake rate has been shown to overcome the avoidance of faeces by grazing herbivores, even in parasitised animals (Hutchings *et al.* 2000b, 2001b). The observation that the selection for tall swards, but not N-rich swards, overcomes faeces avoidance suggests that N intake rate by a grazing herbivore is affected by sward height more than by sward N content. This premise is supported by the finding that sheep can maintain a greater intake of N when they graze N-poor tall swards than when they graze N-rich short swards (Hutchings *et al.* 2000b).

However, in natural systems the spatial and temporal variation in forage resource availability may restrict the opportunity to combat parasites through behaviour (White, 1993; Schetter *et al.* 1998). For example, forage resources may be so low during the winter that hosts cannot meet their nutrient requirements, which represents a major threat to maintaining immunity, and ultimately their survival (Gulland, 1992). During periods of forage scarcity animals may become malnourished and their expression of immunity breaks down (Keusch *et al.* 1983; Barnard & Behnke, 1990). If parasite infection aggravates the state of malnutrition due to food limitation, a vicious circle can be created and mortality can result from a combination of malnutrition and parasitism (McFarlane, 1976; Keymer *et al.* 1983; Gulland, 1992). During periods of time when animals cannot or do not maintain an effective immunity to parasitic infection (e.g. during periods of malnutrition or during the phase of acquisition of immunity), those able to select for plants with anti-parasitic properties for the purpose of self-medication (e.g. to break the vicious circle described earlier) would be at great advantage.

Can parasitised hosts benefit from foods containing anti-parasitic compounds?

Certain plants have been shown to have effective anti-parasitic properties (Guarrera, 1999; Wilkins & Jones, 2000; Adewunmi *et al.* 2001; Baker *et al.* 2001; Deharo *et al.* 2001; Waller *et al.* 2001). The most striking examples of the anti-parasitic properties of plants include extracts of the *Mallotus philippinensis* fruit that can reduce the numbers of cestode eggs excreted in the faeces of goats to an extent similar to that of current levamisole-based anthelmintic drugs (Akhtar & Ahmad, 1992). Similarly, 7 d after an oral administration of papaya (*Catiba papaya*) latex (collected by draining green papaya fruits) pigs parasitised with *Ascaris suum* showed reduced parasitic burdens (up to 100 %; Satrija *et al.* 1994). The anti-parasitic properties of plant extracts, and plants in general, are attributed mainly to plant secondary metabolites (PSM) that have evolved in plants to protect them from depredation by herbivores. These compounds (e.g. phenolic metabolites, N-containing compounds and terpenoids; Harborne, 1991) have a range of impacts on herbivores that include astringency during ingestion, reducing the extent of digestion and toxicity at the tissue level (Rosenthal & Berenbaum, 1991). Given these detrimental effects, it is perhaps not surprising that mammalian herbivores can distinguish plants rich in PSM and where possible they avoid them (Provenza *et al.* 1990; Villalba & Provenza, 2002).

Due to their anti-parasitic properties there is a potential for PSM-rich plant species to be used as alternatives to chemotherapeutic control of parasitism in agricultural systems. Considerable attention has been given recently to the anti-parasitic properties of a class of phenolic metabolites, the condensed tannins (CT), and their effects on gastrointestinal nematode parasites of domestic ruminants. In terms of the anti-parasitic properties of CT, their mode of action on nematode parasites has been found to be mainly a direct anthelmintic effect (Athanasidou *et al.* 2000). The finding that dosing nematode-infected sheep with CT (at

levels found in natural systems, i.e. 8 % food intake) can produce an almost immediate decrease in faecal egg counts (50 %), worm burdens (30 %) and parasite fecundity, indicates the potential magnitude of parasite control that may be achieved. The potential for parasitism to be controlled in domestic ruminants through the use of PSM-rich plant species is further supported by field evidence that gastrointestinal parasitism can be reduced by animals grazing tanniferous forages such as sulla (*Hedysarum corarium*) and *Lotus pedunculatus* (Niezen *et al.* 1998). Evidence of the direct anthelmintic properties of CT suggests that parasitised hosts can benefit from consuming plants with anti-parasitic properties. Furthermore, these potential anti-parasitic benefits of CT, combined with the ability of animals to distinguish plants rich in CT (Provenza *et al.* 1990; Villalba & Provenza, 2002), open up the possibility that they could be exploited for self-medication purposes by the herbivores themselves.

However, the potential benefits associated with the consumption of CT, and indeed any PSM, for parasitised animals must be traded-off against the negative consequences of CT intake on host physiology. In terms of preventing herbivory, the consumption of CT can be associated with impairment of rumen metabolism (a reduction in rumen NH₃ and growth inhibition of rumen microflora) when in the diets of ruminants at >40–50 g/kg DM (Barry & McNabb, 1999). Some types of CT could also detrimentally affect the mucosa of the digestive tract of sheep, and consequently reduce the absorption of organic matter and digestibility of fibre (Reed, 1995; Dawson *et al.* 1999). As a consequence, sheep fed CT have lower growth than those maintained on CT-free diets at the same level of food intake (Reed, 1995; Dawson *et al.* 1999). Given the negative effects of CT on both herbivore hosts and their parasites, there is likely to be a trade-off between the negative consequences for the host of consumption of CT and the positive consequences detailed earlier for the amelioration of parasite burden.

The question then is how could parasitised herbivore hosts associate a potential positive anti-parasitic effect with PSM intake when they avoid PSM-rich plant species? PSM are widespread in plant communities, e.g. tannins alone occur in 79 % of deciduous woody perennials and 87 % of evergreen woody perennials (Bate-Smith & Metcalf, 1957). Whilst herbivores avoid PSM-rich species when given a choice, often they do not have a choice and must make decisions between plants with varying concentrations of PSM (Herrera & Pellmyr, 2002). This factor, combined with the fact that many plant species increase their PSM content as a response to herbivory, results in PSM-containing plant species being a regular component of mammalian herbivore diets (Herrera & Pellmyr, 2002). This regular intake of PSM gives herbivores the opportunity to experience their physiological effects (i.e. detrimental and anti-parasitic effects). There is also the possibility that mammalian herbivores have evolved a hard-wired change in diet selection as a response to parasitism (Kyriazakis *et al.* 1998); for example, parasitised animals could use the bitter taste of PSM-rich plant species (Harborne, 1991) as a cue to the presence of anti-parasitic compounds.

Despite the presence of anti-parasitic compounds, the current evidence that animals self-medicate (i.e. consume plant material that contains anti-parasitic compounds) to ameliorate the effects of parasitism (behaviour 3) is anecdotal and/or equivocal (for review, see Lozano, 1998). Lozano (1998) concluded that experimental research was needed if the concept of self-medication by animals was to be widely accepted. The best evidence for self-medication by animals comes from the primate literature and is based on correlative studies (for reviews, see Lozano, 1998; Engel, 2002; Huffman, 2003). The deficiencies of correlative studies attempting to identify cases of self-medication in primates are due to their inability to establish cause and effect (Lozano, 1998). Also, the logistical and ethical difficulties associated with manipulating the primate–parasite system make it unlikely that self-medication in primates could be demonstrated experimentally, i.e. recording animals self-medicating as a response to experimental parasitic infection (M Huffman, personal communication). Given the recent reviews of the correlative evidence for self-medication by animals, including that of Huffman (2003), attention is focused here on the potential for an experimental approach used to interpret behaviours 1 and 2 in complex environments to be applied to behaviour 3. The potential for herbivores to use PSM to control their parasites is clear; the question, therefore, is whether herbivores use PSM to their advantage. Thus, details are given here of an approach that could be used to provide the needed experimental evidence of self-medication by animals.

The application of trade-off theory to behaviour 3

The trade-off theory may help in the interpretation of the grazing decisions of parasitised hosts that face both positive and negative effects associated with PSM intake. The tri-trophic interaction (CT-rich plant–mammalian herbivore host–gastrointestinal parasite) described earlier may be used to demonstrate self-medication in animals, which may be seen as changes in their PSM intake in relation to their physiological state. For example, when presented with a choice between two foods, one including PSM (e.g. CT) and one without PSM, all else being equal, parasite-naïve hosts would be expected to, and do, avoid the detrimental effects of PSM intake (for example, see Provenza *et al.* 1990). However, parasitised animals, whether in the stage of acquisition or early expression of acquired immunity (i.e. have an existing parasite burden), might be expected to increase their consumption of the PSM for self-medication purposes (Lozano, 1991, 1998). Of course, an increase in PSM intake would only be expected to occur if the anti-parasitic benefits (e.g. the reduction in nutrient loss through parasite-damaged gastrointestinal tissue) outweighed the detrimental costs associated with the PSM intake (e.g. the nutrient costs associated with impairment of rumen metabolism). Finally, a parasite-immune animal (i.e. effective expression of immunity), no longer needing the anti-parasitic effect of PSM might be expected to avoid the PSM once again (Provenza *et al.* 1990). It might then be hypothesised that the PSM intake of a parasite-naïve animal introduced to a parasitised environment can be predicted in relation to the various stages of development of immunity from being

parasite-naive, through to the acquisition phase and finally the expression phase of immunity. Such differences in behaviour in relation to immune state would support the theory that the animals perceive a trade-off and make self-medication foraging decisions on a cost–benefit basis. Naturally-occurring trade-offs between the detrimental and anti-parasitic effects of PSM consumption may be used as a model system in which self-medication could be experimentally demonstrated. It is in such tri-trophic model systems that further research effort should be targeted if self-medication by animals is to be widely accepted.

Conclusion

Parasitised animals are ‘aware’ of their parasitic or immune state and this ‘awareness’ opens up the possibility of combating parasitism through taking advantage of plant properties. In simple environments parasitised mammalian herbivores have the foraging skills to determine and avoid parasite-rich environments and select for increased nutrient intake that may increase their parasite resistance. However, further research is needed to demonstrate that the changes in diet selection seen in response to gastrointestinal parasitism have a positive effect on host resistance to infection and result in decreased levels of parasitism. In more complex environments heterogeneous distributions of forage resources and parasites may coincide, creating nutrition *v.* parasitism trade-offs, and foraging decisions can be expected in relation to its relative costs and benefits. The costs and benefits of the trade-off in grazing systems are affected by the characteristics of the sward and the physiological state of the foraging host. The use of trade-off theory and controlled experimental environments has advanced our understanding of the contact process between hosts and their parasites. A similar approach may be used to further our understanding of self-medication by animals. Current evidence for self-medication by parasitised animals remains equivocal. However, trade-offs between the detrimental and anti-parasitic effects of PSM consumption by animals may be used as a model system to experimentally demonstrate self-medication. It is in such novel tri-trophic (plant–herbivore–parasite) interactions that further research effort should be targeted. Thus, there is strong evidence suggesting that herbivore hosts have developed behaviours to take advantage of plant properties to combat parasites and therefore use foraging behaviour as a weapon in the host–parasite arms race.

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