Proceedings of the Nutrition Society (2003), **62**, 371–381 DOI:10.1079/PNS2003257

Animal self-medication and ethno-medicine: exploration and exploitation of the medicinal properties of plants

Michael A. Huffman
Section of Ecology, Primate Research Institute, Kyoto University, 41–2 Kanrin, Inuyama Aichi 484–8506, Japan

Early in the co-evolution of plant–animal relationships, some arthropod species began to utilize the chemical defences of plants to protect themselves from their own predators and parasites. It is likely, therefore, that the origins of herbal medicine have their roots deep within the animal kingdom. From prehistoric times man has looked to wild and domestic animals for sources of herbal remedies. Both folklore and living examples provide accounts of how medicinal plants were obtained by observing the behaviour of animals. Animals too learn about the details of self-medication by watching each other. To date, perhaps the most striking scientific studies of animal self-medication have been made on the African great apes. The great ape diet is often rich in plants containing secondary compounds of non-nutritional, sometimes toxic, value that suggest medicinal benefit from their ingestion. Chimpanzees (*Pan troglodytes*), bonobos (*Pan paniscus*) and gorillas (*Gorilla gorilla*) are known to swallow whole and defecate intact leaves. The habit has been shown to be a physical means of purging intestinal parasites. Chimpanzees and man co-existing in sub-Saharan Africa are also known to ingest the bitter pith of *Vernonia amygdalina* for the control of intestinal nematode infections. Phytochemical studies have demonstrated a wide array of biologically-active properties in this medicinal plant species. In light of the growing resistance of parasites and pathogens to synthetic drugs, the study of animal self-medication and ethno-medicine offers a novel line of investigation to provide ecologically-sound methods for the treatment of parasites using plant-based medicines in populations and their livestock living in the tropics.

African great apes: Self-medication: Diet: Ethno-medicine: Parasite control

In recent years a growing body of evidence has given momentum to the study of self-medication in animals, often referred to as ‘zoopharmacognosy’ (for example, see Rodriguez & Wrangham, 1993; Huffman, 1997, 2001; Engel, 2002). The amount of detailed information on self-medication in animals gathered thus far is greatest in primates, in particular the African great apes (see Huffman, 1997, 2001). The basic premise of zoopharmacognosy is that animals utilize plant secondary compounds or other non-nutritional substances to combat or control disease. The hypothesis being developed from investigations of self-medication in the great apes is that such behaviour aids in the control of intestinal parasites and provides relief from related gastrointestinal upset (for example, see Huffman *et al*. 1993, 1996*b*; Wrangham, 1995; Huffman & Caton, 2001). However, given the obvious adaptive importance that self-medication implies, it is expected to occur in response to a variety of illnesses throughout the animal kingdom. Parasite infection and other diseases can have a strong effect on the behaviour and reproductive fitness of an individual, making the need to counteract such pressure of extreme importance to survival. Anti-parasitic behaviour is one such adaptive response, with examples ranging from arthropods to primates, and is undoubtedly the product of a long evolutionary process (for example, see Harborne, 1978; Swain, 1978; Blum, 1981; Boppré, 1984; Huffman, 2001). Ethnographic literature and recent ethno-medicinal research suggests that man has long been aware of the use of medicinal plants by animals and has looked to them for clues about the medicinal properties of plants.

The growing problem of antibiotic and anthelmintic resistance is an increasingly serious problem in human health care and livestock husbandry in Africa and around the world. The study of self-medication in nature and tradition-based diet and herbal medicines in man can provide alternative and important insights into dealing with these

Corresponding author: Dr Michael Huffman, fax +81 568 63 538, email huffman@pri.kyoto-u.ac.jp

problems. Detailed behavioural, ethno-medicinal, pharmacological and parasitological investigations are currently underway to elucidate the full potential of self-medication in animals for the prevention and control of illness. Multidisciplinary investigations of chimpanzee behavioural strategies in the wild and ethno-veterinary and ethno-medicinal surveys of traditional African medicine are being conducted by a multi-regional multi-discplinary research consortium, The CHIMPP Group (Huffman, 1994). The present paper reviews some of the literature and recent findings in this area and suggests future directions of research.

Animal self-medication and ethno-medicine

Throughout the history of man animals have been looked to for sources of herbal medicines and narcotic stimulation (for example, see Brander, 1931; Riesenberg, 1948). Anecdotal reports of the possible use of plants as medicine by wild animals such as the elephant, civet, jackal and rhinoceros are abundant (Table 1). The Navajo living in the southwestern USA acknowledge the bear for their knowledge of the antifungal, antiviral and antibacterial properties of the Umbelliferae, *Ligusticum porteri* (Moore, 1979; Grisanzio, 1992).

Tabernanth iboga (Apocynacea) contains several indole alkaloids, and is used as a powerful stimulant and aphrodisiac in many secret religious societies in Gabon (Harrison, 1968). Harrison (1968) speculated that because of the widespread reports from local inhabitants of gorilla (*Gorilla gorilla gorilla*), bush pig and porcupine going into wild frenzies after digging up and ingesting the roots, they probably learned about these peculiar properties of the plant from watching the animals' behaviour. The most active principle, found in the root, is ibogaine, which has been shown to affect the central nervous system and the cardiovascular system. Two other known similarly-active compounds in the plant are tabernanthine and iboluteine. The stimulating effects are similar to those of caffeine (Dubois, 1955). The sloth bear and local population of central India are noted to become intoxicated after eating the fermented madhuca flowers (Brander, 1931) and reindeer and the indigenous Lapps consume fly agaric mushrooms (*Aminita muscaria*) known for their intoxicating effects (Phillips, 1981)

One version of the discovery of coffee is that the chance observation by a shepherd that goats became stimulated after grazing on the berries of wild coffee plants in the highlands of Ethiopia provided the clue for man to exploit the plant as a stimulant. Dr Jaquinto, the trusted physician to Queen Ann, wife of James I in 17th century England, is said to have made systematic observations of domestic sheep foraging in the marshes of Essex, which led to his discovery of a successful cure for consumption (Wilson, 1962). In the foothills of the Himalayas near Mt. Everest the use of the roots of 'chota-chand' as a potent antidote for a snake bite is said to have been learned by observing mongooses feeding on the plant before fighting with cobra (Balick & Cox, 1996). All these examples suggest the occurrence of self-medication in a variety of animal species and ways that man may learn about the medicinal value of plants from them.

Table 1. Some anecdotal evidence for self-medication in animals

Species	Plant specie (Family)	Comments	References
Malay elephant	*Entada schefferi* (Leguminosae):	For stamina before long walk, possible pain killer	Hubback (1941), Janzen (1978)
African elephant	Boraginaceae sp.	Induce labour; used by Kenyan ethnic group to induce labour and abortion. Similar story related to Huffman about observations made in Tanzania	Cowen (1990), MS Kalunde (personal communication)
Indian bison	*Holarrhena antidysenterica* (Apocynaceae)	Bark regularly consumed. Species name suggests anti-dysentaric action	Ogilvie (1929)
Wild Indian boar	*Boerhavia diffusa* (Nyctaginaceae) called pig weed	Roots are selectively eaten by boar and is a traditional Indian anthelmintic	Janzen (1978), Dharmkumarsinhji (1960)
Pigs	*Punicum granatum* (Punicaceae) pomegranate	Root sought after by pigs in Mexico	Janzen (1978), McCann (1932)
		Alkaloid in roots toxic to tapeworms	Caius (1940)
Indian tigers, wild dogs, bears, civets, jackals	*Careya arborea* (Barringtonaeaceae), *Dalbergia latifolia* (Leguminosae) etc.	Fruits of various species eaten by large carnivores. Possibly helps in elimination of parasites ingested along with contents of intestines of herbivore prey	McCann (1932), Burton (1952), Janzen (1978)
South American wolf	*Solanum lycocarpon* (Solanaceae)	Rotting fruit said to be eaten to cure stomach or intestinal upset	DAO Courtnay and GC Kirby (personal communication)
Asiatic two-horned rhinoceros	*Ceriops candoleana* (Rhizophoraceae)	Tannin-rich bark eaten in large amounts enough to turn urine bright orange. Possible use in control of bladder and urinary tract parasites	Hubback (1939)
Black howler monkey, spider monkey		Indigenous peoples living in primate habitats of the Neotropics claim that some monkey species are parasite-free because of the plants they eat	S Vitazkova (personal communication), M Pavelka (personal communication)

https://doi.org/10.1079/PNS2003257 Published online by Cambridge University Press

Table 2. Some common plant secondary compounds and their effects on animals (after Wink *et al.* 1993; Howe & Westly, 1998)

Class of compounds	Effects and comments
Terpenoid alkaloids	Modulation of ion channels (highly toxic)
Isoquinoline alkaloids	DNA intercalation, interaction with receptors, causes spasms (toxic and bitter)
Quinolizidine alkaloids	Binding to ACH receptor (toxic and bitter)
Tropane alkaloids	Inhibition of ACH receptor (highly toxic)
Pyrrolizidine alkaloids	Mutagenic and carcinogenic (liver toxic)
Cyanogenic glycosides	Inhibition of respiration
Cardiac glycosides	Inhibition of Na^+/K^+ -ATPase (highly toxic)
Terpenes	Diuretic (bitter taste)
Volatile terpenes	Antibiotic, irritant
Volatile monoterpenes	Antibiotic (aromatic smell)
Saponines, amines	Detergent for biomembranes (bitter)
Triterpene saponines	Detergent for biomembranes (toxic, emetic)
Sesquiterpenes, pyrrolizidines	PA are mutagenic and carcinogenic, irritant (cytotoxic, liver toxic)
Convallatoxin	Inhibition of Na^+/K^+-ATPase (highly toxic and bitter)
Anthraquinones	Purgative (toxic)
Phenolics	Astringency, reduces digestibility
Cellulose, hemicellulose, lignins, silica	Undigestible

ACH, acetylcholine; PA, pyrrolizidine alkaloids.

Why should any of this information really be a surprise? After all, from an evolutionary standpoint, preservation of health is a basic principle of survival, and all species living today can be expected to have evolved a variety of ways of protecting themselves from predators and parasites, large and small, in their environment.

Where did this process all begin? In the plant world a common line of defence is to produce a variety of toxic secondary compounds such as sesquiterpenes, alkaloids and saponins (Table 2) that prevent predation by animals (for example, see Swain, 1978; Howe & Westley, 1988). At some point in their co-evolutionary history, probably starting with the arthropods, animals began to take advantage of the plant kingdom's protective chemical arsenal to protect themselves from predators and parasites and to enhance their own reproductive fitness (see Blum, 1981). For example, adult danaine butterflies of each gender utilize pyrrolizidine alkaloids for defence against predators, and males have also been shown to depend on it as a precursor for the biosynthesis of a pheromone component needed for courtship (Boppré, 1978, 1984). The monarch butterfly is reported to feed on *Asclepias* species containing cardiac glucosides that make birds sick, conditioning them not to feed on the species (Brower, 1969). Such tri-trophic level interactions are likely to have provided the foundation for the evolution of a more sophisticated level of self-medication seen in the higher vertebrates.

The impact of parasites on the evolution of self-medicative behaviour

Parasitism has played an important role in the evolution of host behaviour throughout the animal kingdom (for example, see Anderson & May, 1982; Futuyma & Slatkin, 1983; Clayton & Moore, 1997). Co-evolution between host and parasite has resulted in the development of mechanisms by which the host limits parasitic infection and the parasite increases its chance of infecting the host (see Hart, 1990; Toft *et al*. 1991; Ewald, 1994). At the primary level, the host's immune response (innate and acquired) normally controls infections. However, some parasites invariably establish themselves by undergoing antigenic variation, thus disguising themselves with the host's antigens, or by interfering directly with the immune response (see Cox, 1993; Wakelin, 1996).

Where physiological adaptation is not enough, hosts have developed behavioural responses to avoid or limit contact with parasites and other pathogens. These behaviours are widespread among vertebrates and include such strategies as regular changing of sleeping or feeding sites and differential use of drinking sites by baboons (*Papio cynocepahalus*) and mangaby monkeys (*Cercocebus albigena*), use of antiparasitic leaf material to line nests or dens occupied over long periods by sparrows and wood rats, and the direct application of aromatic substances to repel fur- and feather-infesting parasites in coatis, capuchin monkeys (*Cebus capucinus*), brown bears, sparrows and starlings (for example, see Kummer cited by Nelson, 1960; Freeland, 1980; Sengputa, 1981; Hausfater & Meade, 1982; Seigstadt cited by Cowen, 1990; Clark, 1991; Grisanzio, 1992; Gompper & Holyman, 1993; Baker, 1996). Learned aversion of foods or tastes associated with illness, parasite infection and compensatory changes in host dietary preferences induced by parasites has been demonstrated in the laboratory and field for a wide range of vertebrates (for example, see Gustavson, 1977; Keymer *et al*. 1983; Kyriazakis *et al*. 1994).

These learned aversions are another level at which the host avoids prolonged exposure to pathogens. Diet modification has also been proposed as a means of altering or controlling internal parasite load. A causal relationship between a sudden change in diet and reduced tapeworm load has been suggested for black bears (Rausch, 1954, 1961). Another example of this type of behaviour involves the ingestion by chimpanzees (*Pan troglodytes*) of specific plant parts (with little or no nutritional value) for their antiparasitic qualities, which may be either pharmacological (Huffman *et al*. 1993, 1998; Ohigashi *et al*. 1994) or physical (Huffman *et al*. 1996*b*; Huffman & Caton, 2001). A discussion of these two behaviours will be presented later (see p. 375).

Food as medicine in animals and man

Many traditional human societies around the world are still very much dependent on plants for both food and medicine. Food and medicine greatly overlap in the diet, sometimes making the difference difficult to perceive. It has been found that 30 % of the plant species identified as foods among the Hausa of Nigeria in western Africa are also used as medicine. Similarly, 89 % of the species they use to treat symptoms of malaria are also used in a dietary context (Etkin & Ross, 1983; Etkin, 1996).

From an evolutionary perspective, it seems likely that many proposed medicinal plants used by animals are derived from the ingestion of rarely eaten or fall-back foods (eaten in periods of main food shortage) with supportive medicinal properties. One of the challenges and difficulties of interpreting self-medication in animals is distinguishing between possible indirect medicinal benefits derived from plants rich in secondary compounds that are assumed to be ingested for their nutritional value *v*. limited and situation-specific ingestion of items that are processed only for their medicinal properties. When consumed on a fairly regular basis throughout the year or in seasons of wide availability, food and medicine may be one in the same. Indeed, in man, many traditional spices, condiments and vegetables of Asian cuisine used today, such as ginger (*Zingiber officinale*) root, marine algae and various herbs contain important sources of anti-tumour agents (Ohigashi *et al*. 1992; Murakami *et al*. 1994, 1996) that may also have an active role in the suppression of parasitic and viral infections.

Many of these 'food–medicines' are beneficial beyond their nutritional value because of the variety of plant secondary compounds they contain. As discussed earlier, these compounds are considered as being produced by the plant to deter herbivores from ingesting them (for example, see Ehrlich & Raven, 1964; Feeny, 1976; Howe & Westley, 1988; Wink *et al*. 1993), but in small amounts such compounds will likely be of some benefit to the consumer. A number of plant foods found in the diet of the great apes appear to share these properties, as can be seen from the diet of Mahale chimpanzees (Fig. 1).

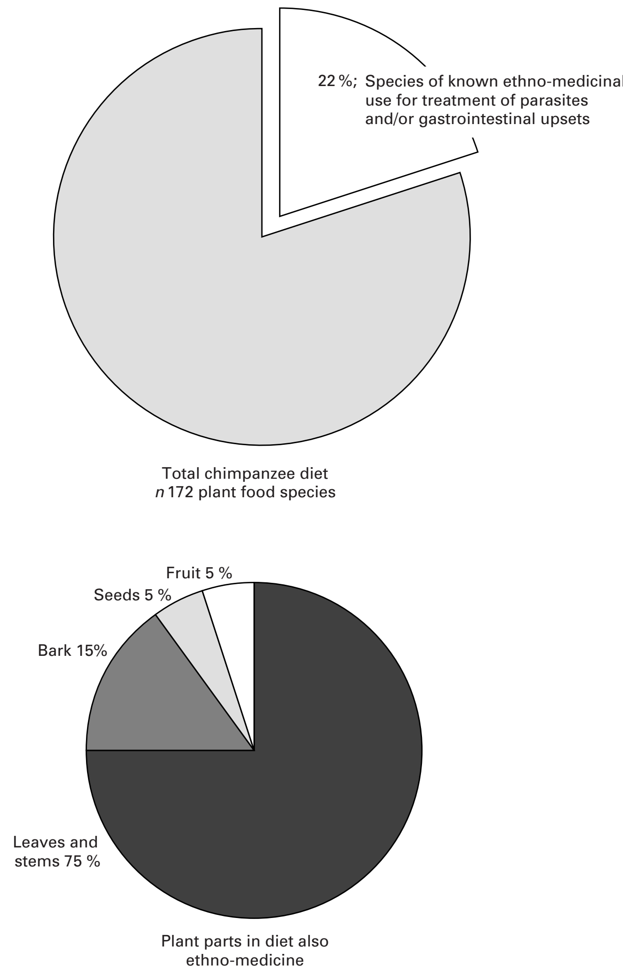

Fig. 1. Percentage contributions and plant parts in the Mahale chimpanzee diet with anthelmintic and other gastrointestinal-relieving properties recognized in the ethno-medicinal and pharmacological literature.

Several species from the genus *Aframomum* are major food plants for gorillas and chimpanzees throughout the lowland rainforests and in many mountain areas (Nishida & Uehara, 1983; Sugiyama & Koman, 1992; Wrangham *et al*. 1993; Idani et al. 1994; Moutsamboté *et al*. 1994; Tutin *et al*. 1994; Yumoto *et al*. 1994). An extensive literature survey of the pharmacological properties of the *Aframomum* by Cousins & Huffman (2002) revealed a wide variety of considerable biological activity, including potent bactericidal activities against *Escherichia coli, Pseudomonas aeruginosa, Yersinia entercolitica, Bacillus subtilis, Proteus vulgaris, Klebsiella pneumoniae* and *Serratia marcescens*. Fungicidal activities inhibited *Candida albicans, Trichophyton mentagrophytes, Aspergillus niger, Botryodiplodis theobromae* and species of *Cladosporium cladosporiodes* (Oloke *et al*. 1988). Bioassays of the extract of *Aframomum danielli* have been made by Adegoke & Skura (1994), revealing active growth inhibitors of *Salmonella enteriditis, Pseudomonas fragi, Pseudomonas fluorescens, Proteus vulgaris, Streptococcus pyogens, Staphylococcus aureus, Aspergillus flavus, Aspergillus parasiticus, Aspergillus ochraceus* and *A. niger*.

The berries of *Phytolacca dodecandra* L. Herit (Phytolaccaceae) are an abundant and frequently-ingested food item of the Kanyawara group of chimpanzees in Kibale, western Uganda (Wrangham & Isabirye-Basuta cited by Huffman & Wrangham, 1994). These bitter-tasting berries are a concentrated source of at least four toxic triterpenoid saponins (lemmatoxin, lemmatoxin-C, oleanoglycotoxin-A, phytolacca-dodecandra glycoside). Consumption of about 2 g of the material is fatal in mice and rats. Other known properties of these triterpinoid saponins include antiviral, antibacterial, anti-fertility, spermicidal and embryotoxic activities (Kloos & McCullough, 1987).

The tips of the young leaves of *Thomandersia laurifolia* (*T. Anders*. ex Benth.) Baill. (Acanthaceae) are on rare occasions chewed by western lowland gorillas in the Ndoki

https://doi.org/10.1079/PNS2003257 Published online by Cambridge University Press

forest of northern Congo (S Kuroda, personal communications). According to Kuroda and colleagues, the local human inhabitants use these leaves as a treatment for parasites and fever. Weak anti-schistosomal activity has been found from crude leaf extracts (Ohigashi, 1995).

Bark and wood are characteristically highly fibrous, heavily lignified, sometimes toxic, relatively indigestible and nutrient poor (Waterman, 1984). Chimpanzees and gorillas are known to infrequently ingest the bark and wood of several plant species (for example, see Huffman & Wrangham, 1994).

While the list of plant species whose bark is ingested is extensive, little is actually known about the contribution of bark to the diet and general health. The literature on African ethno-medicine suggests some medicinal benefits from its consumption. The bark of *Pycnanthus angolensis* (Welw.) Warb. (Myristicaceae) avidly ingested by chimpanzees at Mahale in western Tanzania is used by West Africans as a purgative, laxative, digestive tonic, emetic and reliever of toothaches (Abbiw, 1990). In Tanzania the chimpanzees of Gombe National Park occasionally eat the bark of *Entada abyssinica* Steud. ex A. Rich. (Mimosaceae). In Ghana the bark is used by the human population to treat diarrhoea and as an emetic (Abbiw, 1990). The bark of *Erythrina abyssinica* DC (Papilionacea) is occasionally eaten by Mahale chimpanzees. Marked plasmodicidal and anti-schistosomal activities have been demonstrated for the bark of this species collected at Mahale (Ohigashi, 1995; C Wright, C Phillipson, DV Kirby, MA Huffman and H Ohigashi, unpublished results). The bark of *Gongronema latifolium* Benth. (Asclepiadaceae) occasionally eaten by the chimpanzees of Bossou Guinea is extremely bitter, and the stems are used by the human population in West Africa as a purge for colic, stomach pains and symptoms connected with intestinal parasite infection (Burkill, 1985).

The present brief overview of some of the fruit, leaf, bark and wood items ingested by the great apes serves to demonstrate the diversity of secondary compounds or inferred pharmacological activity present in their diet. The total effect of ingesting these items is still unclear, but it is unrealistic to assume nutritional gain alone as the utility of ingestion when little nutritional value is likely to be obtained.

Use of plants as medicine by chimpanzees in the wild

Recent evidence from the African great apes suggests that certain plants are ingested, not incidentally but directly, for their considerable medicinal value. The hypothesis currently being developed is that the behaviours aid in the control of intestinal parasites (*Oesophagostomum stephanostomum, Bertiela sturdi*) and/or provide relief from related gastrointestinal upset (Wrangham, 1995; Huffman *et al*. 1996*b*; Huffman, 1997; Dupain *et al*. 2002). These observations provide the clearest systematic evidence collected thus far for self-medication in animals. Perhaps due to their phylogenetic closeness, man and chimpanzees select some of the same plants when displaying similar symptoms of illness (Huffman *et al*. 1996*a*). Unquestionably, the implications of self-medicative behaviour are of extreme interest when considering the nutritional and medicinal habits during the evolution of great apes, early hominids and *Homo sapiens*.

Whole-leaf swallowing and the physical expulsion of parasites

The first documentation of a putative self-medicative behaviour in the great apes is known as leaf-swallowing behaviour. It was the lack of any apparent nutritional value in swallowing leaves whole that brought this behaviour to the attention of primatologists (Wrangham & Nishida, 1983). Leaves are frequently swallowed early in the morning, often as the first, or one of the first, items ingested (Wrangham & Nishida, 1983; Wrangham & Goodall, 1989; Huffman *et al*. 1997; Huffman & Caton, 2001). Leaf swallowing is the slow and deliberate swallowing, one at a time, of whole leaves that are folded between tongue and palate, and pass through the gastrointestinal tract visibly unchanged.

Initially, the self-medicative value of leaf swallowing and the possible link between the behaviour and parasite expulsion was not recognized. A chemical action was first proposed *ad hoc* on the basis of the ethno-medicinal uses of species in the genus *Aspilia*, the first observations being documented by Wrangham & Nishida (1983). Subsequently, preliminary chemical analysis of plant material led researchers to propose an antibiotic and/or nematocidal component to the behaviour (Rodriguez *et al*. 1985; Rodriguez & Wrangham, 1993). This hypothesis has since been rejected in light of more extensive and detailed studies in the laboratory that have failed to replicate the earlier results (Page *et al*. 1992, 1997; Huffman *et al*. 1996*b*; Messner & Wrangham, 1996). Field observations have positively linked leaf swallowing with the expulsion of parasites (Wrangham, 1995; Huffman *et al*. *1996b*), but its mode of action is considered to be largely a physical one, in which parasites are purged from the host by means of self-induced reduction in gut transit time and diarrhoea (Huffman & Caton, 2001). Independent analysis of this behaviour in two populations of eastern long-haired chimpanzees (*Pan troglodytes schweinfurthii*) has reported a correlation between the swallowing of whole leaves and the expulsion of the strongyle nematode O. *stephanostomum* at Mahale, Tanzania, and a species of the tapeworm (*Bertiella studeri*) at Kibale, Uganda (Wrangham, 1995; Huffman *et al*. *1996b*).

Leaf-swallowing behaviour is now known to occur widely in the African great apes. Chimpanzees, bonobos (*Pan paniscus*) and lowland gorillas use a wide range of plant genera, represented by more than thirty-four species (Huffman, 1997, 2001). Evidence suggests that similar behaviour may also have evolved convergently in at least two other different vertebrate taxa; the snow goose (*Anser caerulescens*) and brown bear (see Huffman, 1997).

Vernonia amygdalina *and bitter-pith chewing behaviour*

The hypothesis that bitter-pith chewing has medicinal value for chimpanzees was first proposed after detailed behavioural observations and parasitological and phytochemical analyses of patently-ill chimpanzees ingesting *Vernonia*

https://doi.org/10.1079/PNS2003257 Published online by Cambridge University Press

amygdalina Del. (Compositae) at Mahale (Huffman & Seifu, 1989; Huffman *et al*. 1993). These observations are the first reported systematic observations to verify illness and subsequent improvement in health of an animal ingesting medicinal plants.

V. amygdalina occurs throughout tropical sub-Saharan Africa (Watt & Breyer-Brandwijk, 1962). Bitter-pith chewing of other *Vernonia* species has been observed at Gombe, Tanzania (*V. colorata* (Willde.) Drake; Huffman & Wrangham, 1994; Hilali, unpublished results cited by J Wallis, personal communication) and Kahuzi-Biega, Congo-Kinshasa (*V. hochstetteri* Schi-Bip., *V. kirungae* Rob. E. Fries; Yumoto *et al*. 1994; AK Basabose, personal communication). At Tai, Ivory Coast, the bitter piths of *Paliosota hirsuta* (Thunb.) K. Schum. (Commelinacae) and *Eremospath macrocarpa* (Mann & Wendl.) Wendl. (Palmae) are chewed (C Boesch, personal communication cited by Huffman, 1997).

When ingesting the pith from young shoots of *V. amygdalina*, chimpanzees meticulously remove the outer bark and leaves to chew on the exposed pith, from which they extract the extremely bitter juice and residual amounts of fibre. The amount of pith ingested in a single bout is relatively small, ranging from portions of 50–1200 mm × 10 mm. The entire process, depending on the amount ingested, can take from <1 to 8 min. Mature conspecifics in proximity to an individual chewing *Vernonia* bitter pith or leaf swallowing show little or no interest in ingesting the pith (Huffman & Seifu, 1989; Huffman *et al*. 1997), but will on occasion approach the individual and watch it. Infants have been observed to taste the pith discarded by their ill mothers. Interestingly, one instance of a healthy mother refusing her infant access to the discarded pith of an ill chimpanzee has also been observed at Mahale (MA Huffman, unpublished results). In this way, group individuals are exposed to both the behaviour and the extremely bitter taste of the pith from a very young age.

At Mahale, use of *V. amygdalina* has been recorded in all months except June and October (late dry season), demonstrating its year-round availability (Nishida & Uehara, 1983). However, despite this factor, its use by chimpanzees is highly seasonal. It is most often used during the rainy season months of December and January, the time when parasite re-infection by *O. stephanostomum* and other nematodes is at their peak (Huffman *et al*. 1997).

The ethno-medicine and phytochemistry of bitter-pith chewing

V. amygdalina is used by numerous African ethnic groups across the continent as medicine (Table 3). A concoction made from this species is prescribed treatment for malarial fever, schistosomiasis, amoebic dysentery, several other intestinal parasites and stomach-aches, and a variety of other ailments (Dalziel, 1937; Watt & Breyer-Brandwijk, 1962; Burkill, 1985; Huffman *et al*. 1996*a*). The Tongwe of Mahale use this plant as a treatment for intestinal parasites, diarrhoea and stomach upset.

Phytochemical analysis of *V. amygdalina* samples collected at Mahale from plants that are known to be used by chimpanzees revealed the presence of two major classes of bioactive compounds. A total of four known sesquiterpene lactones, seven new stigmastane-type steroid glucosides and two freely-occurring aglycones of these glucosides have been isolated by our group (Ohigashi *et al*. 1991; Jisaka *et al*. 1992*a,b*, 1993*a,b*). The sesquiterpene lactones present in *V. amygdalina*, also found in *V. colorata* and a number of other *Vernonia* spp., are well known for their anthelmintic, anti-amoebic, anti-tumour and antibiotic properties (Toubiana & Gaudemer, 1967; Kupchan *et al*. 1969; Asaka *et al*. 1977; Gasquet *et al*. 1985; Jisaka *et al*. 1992*a*, 1993*b*). From crude methanol extracts of the leaves Koshimizu *et al*. (1993) also found inhibition of tumour promotion and immuno-suppressive activities.

In vitro tests on the anti-schistosomal activity of the pith's most abundant steroid glucoside (vernonioside B_1), and sesquiterpene lactone (vernodaline), showed marked inhibition of movement of the adult parasites and adult females' egg-laying capacity (Jisaka *et al*. 1992*b*). These findings are consistent with the observed decline (from 130 to fifteen eggs per g faeces; 88 % decrease) in the *O. stephanostomum* faecal egg count level measured 20 h after an adult female chimpanzee at Mahale ingested *V. amygdalina* pith. The normal egg count fluctuation recorded during the same period for seven other individuals was an increase in egg count of 69·9 (SD 84, range 5–236; Huffman *et al*. 1993). The sesquiterpene lactones showed marked *in vivo* plasmodicidal activity, while that of the steroid glucosides was weaker (Ohigashi *et al*. 1994). *In vivo* test trials of *V. amygdalina* by Nfi *et al*. (1999) validated the ethno-veterinary use of this plant by Fulani pastoralists as an anthelmintic, observing >52 % reduction in faecal egg count for nematodes, including *Oesophagostomum* spp. following treatment with a decoction.

Some of the species with bitter piths ingested by chimpanzees at Gombe, Kahuzi-Biega and Tai also have a number of ethno-medicinal and pharmacological properties. *V. colorata* and *V. amygdalina* are not distinguished from each other ethno-medicinally in relation to their medicinal properties and folk classification (Burkill, 1985). Alkaloids occur in the pith, as well as flower and leaf of *V. hochstetteri* (Smolenski *et al*. 1974). *P. hirsuta* and *E. macrocarpa* are used in west African ethno-medicine for the treatment of upset stomachs, colic, as an antiseptic and analgesic, and for venereal disease (Abbiw, 1990; Neuwinger, 1996). Moluscicidal activity has also been reported for *P. hirsuta* (Okunji & Iwu, 1988).

A link between animal self-medication and ethno-medicine

The ethno-medicinal uses of *V. amygdalina* and the conditions under which ill chimpanzees have been observed to ingest this species are similar in many respects (Huffman *et al*. 1993, 1996*a*). In the two most detailed documented cases of use by chimpanzees described earlier, the rate of recovery (20–24 h) was comparable with that of indigenous human inhabitants of Mahale and neighbouring regions (within 24 h), who use *V. amygdalina* for the treatment of parasitosis and gastrointestinal upset.

This group, the Tongwe, typically make their medicine from a cold-water decoction of two to three crushed fresh leaves (approximately 10–15 g fresh weight) in 300–400 ml water. Due to the plant's toxic effect on the patient, this treatment typically comprises one dose, but smaller amounts spread over the day(s) are sometimes also prescribed (MS Kalunde, personal communication). An analysis replicating this traditional method (three trials) yielded 3·3–5·0 mg vernonioside B1 (Huffman *et al*. 1993). This finding was compared directly with chimpanzee intake by quantitative analysis of pith collected from the plant used by the adult female chimpanzee that had experienced a drop in parasite load 20 h after its ingestion. The amount of pith she ingested (600 mm, approximately 50–100 g fresh weight) was found to contain approximately 3·8–7·6 mg vernonioside B1; an amount approximately equal to that normally obtained by a Tongwe patient in a single full dose (Huffman *et al*. 1993).

Both man and chimpanzees appear to recognize the important physiological activity of this plant, and evidence suggests that chimpanzees ingest *V. amygdalina* when they experience some of the same symptoms. From an ethno-botanical viewpoint, the greater number of different cultures that recognize a single plant species as having some kind of medicinal property, the more likely that species is to contain marked physiological activity. The example of *V. amygdalina*, with its widely-recognized medicinal value in Africa, takes this process one step further by bridging the gap between apes and man (Table 3).

Tongwe ethno-zoology and health care

A key collaborator in my long-term research at Mahale is Tanzanian National Park game officer Mohamedi Seifu

Table 3. Ethno-medicinal uses of *Vernonia amygdalina* in Africa*

Application	Plant part used	Region used	Comments
General intestinal upsets:			
Enteritis	Root, seeds	Nigeria	
Constipation	Leaves, sap	Nigeria, Tanzania, Ethiopia	As a laxative
Diarrhoea	Stem, root bark, leaves	West Africa, Zaire	
Stomach upset	Stem, root bark, leaves	Angola, Ethiopia	
Parasitosis:			
Schistosomiasis	Root, bark, fruit	Zimbabwe, Mozambique, Nigeria	Sometimes mixed with *Vigna sinensis*
Malaria	Root, stem bark, leaves	East Africa, Angola, Guinea, Nigeria, Ethiopia	A quinine substitute
Trematode infection	Root, leaves	East Africa	Treatment for children used as a suppository
Amoebic dysentery	Root bark	South Africa	
Ringworm	Leaves	Nigeria	Ringworm and other unidentified epidermal infections
Unspecified	Leaves	Nigeria	Prophylactic treatment for nursing infants, passed through mother's milk
	Root, seeds	Nigeria	Worms
	Leaves	West Africa	Crushed in water and given to horses as a vermifuge, livestock fodder supplement for treating worms
	Leaves	Ghana	Purgative
Tonic food	Leaves	Cameroon, Nigeria	Boiled or soaked in cold water, prepared as soup or as a vegetable fried with meat, 'n'dole', 'fatefate', 'mayemaye', leaves sold in markets and cultivated in home gardens
Other ailments:			
Amenorrhoea	Root	Zimbabwe	
Coughing	Leaf	Ghana, Nigeria, Tanzania	
Diabetes	All bitter parts	Nigeria	
Fever	Leaves	Tanzania, Kenya, Uganda, Congo-Kishasa	Leaves squeezed and juice taken
Gonorrhoea	Roots	Ivory Coast	Taken with *Rauwolfa vomitoria*
'Heart weakness'	Root	West Africa	Vernonine is a cardiotonic glycoside comparable with digitalin
Lack of appetite	Leaf	West Africa	Leaves soaked in cold water to remove bitterness and then boiled in soup
Pneumonia	Leaf	Ivory Coast	Taken with *Argemone maxicana* or used in a bath
Rheumatism	Stem, root bark	Nigeria	
Scurvy	Leaves	Sierra Leone, Nigeria, West Cameroon	Leaves sold in markets and cultivated in home gardens
General hygiene:			
Dentrifice	Twig, stick	Nigeria	Chew stick for cleansing and dental caries
Disinfectant	Not given	Ethiopia	
Soap	Stems	Uganda	

*Data from Dalziel (1937), Irvine (1961), Watt & Breyer-Branwijk (1962), Kokwaro, (1976), Palgrave (1983), Burkill (1985), Abebe (1987), Nyazema (1987), Akah & Okafor (1990), Muanza, *et al*. (1993), Huffman, unpublished results from interviews in Uganda and Tanzania.

https://doi.org/10.1079/PNS2003257 Published online by Cambridge University Press

Kalunde, who comes from a long family line of traditional healers. During the course of collaborative work starting in 1987, he has taught me much about the medicinal plants used by his people, the Tongwe, some of which are also found in the diet of chimpanzees in the Mahale M group. His narratives have provided me with important insights into the origins of some of the Tongwe's most important medicinal treatments, notably acquired through the observation of sick wild animals such as the elephant, porcupine and bush pig.

An example is 'munyonga nTembo', which is used by the Tongwe as a treatment for general stomach upsets. The leaves are crushed and placed in water. The resulting solution is drunk or the crushed leaves are used as a suppository. The origin of the use of this plant for medicinal purposes has been preserved in its name. The Tongwe verb 'kunyonga' means to twist and pull off. Elephants (tembo in both Swahili and Tongwe) twist and pull off the leaves of this plant before ingesting them. It is said that one day an elephant visibly suffering from stomach upset was observed obtaining a bunch of leaves from this particular species. The elephant put a few bunches of leaves in its mouth, and after chewing on them a bit, drew up some water and blew it into its mouth. After holding the water in its mouth together with the leaves for sometime, it blew the leaves out of its nose and swallowed the water. The observer interpreted the elephant's behaviour as using a cold-water concoction from the leaves. The leaves of this plant are thus prepared as a Tongwe treatment for stomach upset.

Another important medicinal plant of the Tongwe, 'mulengele' (*Aeschynomene* sp., Leguminosae), was first discovered by Mohamedi's grandfather, babu Kalunde, as a treatment for diarrhoea with blood, from watching a sick young porcupine ingest the roots of this plant and recover from these symptoms. The story goes as follows. On one occasion babu Kalunde was out checking his snares for captured prey. He came upon a female porcupine in one of them. He killed the porcupine, but found out too late that she had dependent young hidden in the bush nearby. Babu Kalunde took the young home to care for them. He put them in a small enclosure so that they would not stray off. The young porcupines grew ill with passing time, displaying, among other symptoms, bloody diarrhoea. These symptoms were the same as those showing up in members of the village, and babu Kalunde was looking for something with which to cure them. During this time one of the ill porcupines escaped and wandered off into the forest. Following it to see what it would do, babu Kalunde observed it dig up and chew on the roots of mulengelele. The species had never been used as medicine before, but was known and avoided because of its highly toxic qualities. He observed that the porcupine became better over time, convincing babu Kalunde that he should try it on the sick people of his village. He told the villagers what he had seen and asked to be allowed to test it on the sick. People were at first reluctant because of the plant's reputation, but it was agreed that if babu Kalunde himself would first take some they too would submit to treatment. He took a small decoction and they were satisfied. The medicine was put to work to cure many people in the village afflicted with bloody diarrhoea. From that time the plant has become an important medicine of the Tongwe in regions of western Tanzania where the plant is found.

Mohamedi has experimented with the plant on various illnesses and has also found it effective against syphilis and gonorrhoea. It has also recently been learned that a traditional healer in Mpanda, western Tanzania, has used the root to treat AIDS-related symptoms. All this evidence suggests that the plant may possess marked antibiotic activity. Laboratory investigations are currently underway to determine the types of compounds present in the roots and to ascertain their pharmacological properties.

Mohamedi's mother, Joha Kasante, also a traditional healer, experimented with an antidote for snake bite by asking Mohamedi to follow the snake that bit his younger brother and bring back leaves of the plant that the snake subsequently chewed on. The leaves are said to prevent the snake's venom from circulating throughout the body. After chewing on the leaves his brother immediately vomited, but suffered no further ill consequences from the snake bite. Separated by great distances and cultures, this story closely resembles that of 'chota-chand' from the Himalayas of Nepal, noted earlier. Is this similarity a coincidence, or have populations around the world obtained similar knowledge from watching the behaviour of similar animal species? Given the fact that animals of the same or similar species and genera distributed around the globe share behavioural traits in common with one another, this explanation does seem to be possible. For example, the leaf-swallowing habit of bears is reported to occur in Eurasia and North America (see Huffman, 1997).

Future studies and directions of research

As the present paper has shown, the disciplines of animal behaviour, parasitology, pharmacognosy and ethno-medicine have the unique potential to provide important leads to future sources of nutriceuticals and medicine for the control and/or treatment of parasitosis, together with a number of other interesting possibilities. In addition, a closer look into the manner in which animals use natural plant products in combination with antiparasitic behaviour may provide new insights into alternative strategies for suppressing or slowing down the rate of acquisition of chemo-resistance by these parasites in livestock and human populations living in the tropics.

The next step in this research is to conduct *in vivo* tests to determine direct efficacy in a wide range of parasites, using a number of different host species. Differences in metabolism, drug pharmacokinetics etc. between single-stomached animals and ruminant livestock necessitates screening activities in a broad range of animal species. Protocols for testing herbal preparations against the nematode parasites of economically-important farm animals (both ruminant and single-stomached animals) as a model system would be of great benefit to agricultural sectors around the world.

This multi-disciplinary approach to research, in which biological activity of novel plant-derived compounds acquired from the study of animal behaviour and ethno-medicine are assessed against a whole range of parasite species found across a wide range of hosts, maximizes the chance of success. Contributions from multiple disciplines and cultural traditions to the study of animal self-medication and ethno-pharmacology can bring about a rich understanding and appreciation of the value of Africa's cultural and biological diversity for the future of its population, as well as science in general. An ultimate objective of this research is to integrate our results into local health care and livestock management systems so that locally-available plants can be properly used to the benefit of all.

Acknowledgements

The author wishes to thank the many collaborators and their institutions around the world for untiring support, intellectual input and friendship. There are too many to name them all here, but I wish to thank in particular Guy Balansard, Mohamedi S. Kalunde, the late Junichiro Itani, Hosey Kayumbo, Mayunga H.H. Nkunya, Koichi Koshimizu, Charles Nshimo, Hajime Ohigashi, Ton Polderman, Shunji Gotoh and the following institutions: Kyoto University; Tanzanian National Parks; Tanzanian Commission for Science and Technology; Tanzania Wildlife Research Institute; Japan Ministry of Education, Science, Culture and Sports; the Wellcome Trust, UK; Louis Pasteur Institute, Kyoto, Japan; the Leakey Foundation. Without them, this paper could not have been written.

References

Abbiw DK (1990) *Useful Plants of Ghana*. Kew: Intermediate Technology Publications and Royal Botanic Gardens.

Abebe D (1987) Plants in the health care delivery system of Africa. In *Medicinal and Poisonous Plants of the Tropics*, pp. 79–87 [AJM Leeuwenburg, compiler]. Wageningen: Pudoc Wageningen.

Adegoke GO & Skura BJ (1994) Nutritional profile and antimicrobial spectrum of the spice *Aframomum danielli*. *Plant Foods for Human Nutrition* **45**, 175–182.

Akah PA & Okafor CL (1990) Blood sugar lowering effects of *Vernonia amydgalina* in experimental rabbit model. In *The State of Medicinal Plant Research in Nigeria. Integrative Seminar on Natural Products Research and Development of Plant Based Drugs*, p. 27 [A Sofowora, editor]. Kumani, Ghana: University of Science and Technology.

Anderson RM & May RM (1982) *Population Biology of Infectious Diseases*. Berlin: Springer-Verlag.

Asaka Y, Kubota T & Kulkrani AB (1977) Studies on a bitter principle from *Vernonia anthelmintica*. *Phytochemistry* **16**, 1838–1839.

Baker M (1996) Fur rubbing: Use of medicinal plants by capuchin monkeys (*Cebus capucinus*). *American Journal of Primatology* **38**, 263–270.

Balick MJ & Cox PA (1996) *Plants, People, and Culture*. New York: WH Freeman and Co.

Blum MS (1981) *Chemical Defenses of Arthropods*. New York: Academic Press.

Boppré M (1978) Chemical communication, plant relationships, and mimicry in the evolution of danaid butterflies. *Applied Experimental Entomology* **24**, 264–277.

Boppré M (1984) Redefining 'Pharmacophagy'. *Journal of Chemical Ecology* **10**, 1151–1154.

Brander AAD (1931) *Wild Animals in Central India*. London: Edward Arnold.

Brower LP (1969) Ecological chemistry. *Scientific American* **22**, 22–29.

Burkill HM (1985) *The Useful Plants of West Tropical Africa*, vol. 1, 2nd ed. Kew: Royal Botanical Gardens.

Burton RW (1952) The tiger as fruit eater. *Journal of the Bombay Natural History Society* **50**, 649.

Caius JF (1940) The pomegranite. *Journal of the Bombay Natural History Society* **42**, 13–37.

Clark CC (1991) The nest protection hypothesis: the adaptive use of plant secondary compounds by European starlings. In *Bird-parasite Interactions: Ecology, Evolution, and Behaviour*, pp. 205–221 [JE Loye and M Zuk, editors]. Oxford: Oxford University Press.

Clayton DH & Moore J (1997) *Host-parasite Evolution. General Principles & Avian Models*. Oxford: Oxford University Press.

Cousins D & Huffman MA (2002) Medicinal properties in the diet of gorillas – an ethnopharmacological evaluation. *African Study Monographs* **23**, 65–89.

Cowen R (1990) Medicine on the wild side. *Science News* **138**, 280–282.

Cox FEG (1993) *Modern Parasitology*, 2nd ed. Oxford: Blackwell Scientific Press.

Dalziel JM (1937) *The Useful Plants of West Tropical Africa. Appendix to Flora of West Tropical Africa* [J Hutchinson and JM Dalziel, editors]. London: Whitefriars Press.

Dharmakumarsinhji RS (1960) Indian wild boar (*Sus scrofa cristatus* Wagner) feeding on *Boerhavia diffusa* Linn. *Journal of the Bombay Natural History Society* **57**, 654–655.

Dubois L (1955) Tabernanthe Iboga Baillon. *Bulletin Agricole du Congo Belgique* **46**, 805–829.

Dupain J, Van Elsacker L, Nell C, Garcia P, Ponce F & Huffman MA (2002) New evidence for leaf swallowing and *Oesophagostomum* infection in bonobos (*Pan paniscus*). *International Journal of Primatology* **23**, 1053–1062

Ehrlich P & Raven PH (1964) Butterflies and plants: A study in coevolution. *Evolution* **18**, 586–608.

Engel C (2002) *Wild Health*. Boston, MA: Houghton Mifflin.

Etkin NL (1996) Medicinal cuisines: diet and ethnopharmacology. *International Journal of Pharmacology* **34**, 313–326.

Etkin NL & Ross PJ (1983) Malaria, medicine, and meals: Plant use among the Hausa and its impact on disease. In *The Anthropology of Medicine: From Culture to Method*, pp. 231–259 [L Romanucci-Ross, DE Moerman and LR Tancredi, editors]. New York: Praeger.

Ewald PW (1994) *Evolution of Infectious Disease*. Oxford: Oxford University Press.

Feeny P (1976) Plant apparency and chemical defense. *Recent Advances in Phytochemistry* **10**, 1–40.

Freeland WF (1980) Mangaby (*Cercocebus albigena*) movement patterns in relation to food availability and fecal contamination. *Ecology* **61**, 1297–1303.

Futuyma DJ & Slatkin M (1983) *Coevolution*. Sunderland, MA: Sinauer Associates Inc.

Gasquet M, Bamba D, Babadjamian A, Balansard G, Timon-David P & Metzger J (1985) Action amoebicide et anthelminthique du vernolide et de l'hydroxyvernolide isoles des feuilles de *Vernonia colorata* (Willd.) Drake (Amoebicidal and anthelmintic action of vernolide and hydroxyvernolide isolates of the leaves of *Vernonia colorata* (Willd.) Drake). *European Journal of Medical Chemical Theory* **2**, 111–115.

Gompper ME & Holyman AM (1993) Grooming with *Trattinnickia* resin: possible pharmaceutical plant use by coatis in Panama. *Journal of Tropical Ecology* **9**, 533–540.

Grisanzio JA (1992) Fur-bearing pharmacists. *Animals* September–October issue, 26–30.

Gustavson CR (1977) Comparative and field aspects of learned food aversions. In *Learning Mechanisms in Food Selection*,

pp. 23–43 [LM Barker, MR Best and M Domjan, editors]. Baylor, TX: Baylor University Press.
Harborne JB (editor) (1978) *Biochemical Aspects of Plant and Animal Coevolution. Phytochemical Society of Europe Symposia Series* no. 15. London: Academic Press.
Harrison GP (1968) *Tabernanthe iboga*: an African narcotic plant of social importance. *Economic Botany* **23**, 174–184.
Hart BL (1990) Behavioral adaptations to pathogens and parasites: Five strategies. *Neuroscience and Biobehavioral Review* **14**, 273–294.
Hausfater G & Meade BJ (1982) Alternation of sleeping groves by yellow baboons (*Papio cynocepahalus*) as a strategy for parasite avoidance. *Primates* **23**, 287–297.
Howe HF & Westley LC (1988) *Ecological Relationships of Plants and Animals*. Oxford: Oxford University Press.
Hubback TB (1939) The two-horned Asiatic rhinoceros (*Dicerorhinus sumatrensis*). *Journal of the Bombay Natural History Society* **40**, 594–617.
Hubback TB (1941) The Malay Elephant. *Journal of the Bombay Natural History Society* **42**, 483–509.
Huffman MA (1994) The C.H.I.M.P.P. Group: A multi-disciplinary investigation into the use of medicinal plants by chimpanzees. *Pan Africa News* **1**, 3–5.
Huffman MA (1997) Self-medication in primates. *Yearbook of Physical Anthropology* **40**, 171–200.
Huffman MA (2001) Self-medicative behavior in the African Great Apes – an evolutionary perspective into the origins of human traditional medicine. *BioScience* **51**, 651–661.
Huffman MA & Caton JM (2001) Self-induced increase of gut motility and the control of parasitic infections in wild chimpanzees. *International Journal of Primatology* **22**, 329–346.
Huffman MA, Gotoh S, Izutsu D, Koshimizu K & Kalunde MS (1993) Further observations on the use of *Vernonia amygdalina* by a wild chimpanzee, its possible effect on parasite load, and its phytochemistry. *African Study Monographs*. **14**, 227–240.
Huffman MA, Gotoh S, Turner LA, Hamai M & Yoshida K (1997) Seasonal trends in intestinal nematode infection and medicinal plant use among chimpanzees in the Mahale Mountains, Tanzania. *Primates* **38**, 111–125.
Huffman MA, Koshimizu K & Ohigashi H (1996*a*) Ethnobotany and zoopharmacognosy of *Vernonia amygdalina*, a medicinal plant used by humans and chimpanzees. In *Compositae: Biology & Utilization*, vol. 2, pp. 351–360 [PDS Caligari and DJN Hind, editors]. Kew: The Royal Botanical Gardens.
Huffman MA, Page JE, Sukhdeo MVK, Gotoh S, Kalunde MS, Chandrasiri T & Towers GHN (1996*b*). Leaf-swallowing by chimpanzees, a behavioral adaptation for the control of strongyle nematode infections. *International Journal of Primatology* **17**, 475–503.
Huffman MA & Seifu M (1989) Observations on the illness and consumption of a possibly medicinal plant *Vernonia amygdalina* (Del.), by a wild chimpanzee in the Mahale Mountains National Park, Tanzania. *Primates* **30**, 51–63.
Huffman MA & Wrangham RW (1994) The diversity of medicinal plant use by chimpanzees in the wild. In *Chimpanzee Cultures*, pp. 129–148 [RW Wrangham, WC McGrew, FB DeWaal and PG Heltne, editors]. Cambridge, MA: Harvard University Press.
Idani G, Kuroda S, Kano T & Asato R (1994) Flora and vegetation of Wamba Forest, Central Zaire with reference to Bonobo (*Pan paniscus*) foods. *TROPICS* **3**, 309–332.
Irvine FR (1961) *Woody Plants of Ghana*. London: Oxford University Press.
Janzen DH (1978) Complications in interpreting the chemical defenses of tree against tropical arboreal plant-eating vertebrates. In *The Ecology of Arboreal Folivores*, pp. 73–84 [GG Montgomery, editor]. Washington, DC: Smithsonian Institute Press.
Jisaka M, Kawanaka M, Sugiyama H, Takegawa K, Huffman MA, Ohigashi H & Koshimizu K (1992*a*) Antischistosomal activities of sesquiterpene lactones and steroid glucosides from *Vernonia amygdalina*, possibly used by wild chimpanzees against parasite-related diseases. *Bioscience, Biotechnology and Biochemistry* **56**, 845–846.
Jisaka M, Ohigashi H, Takagaki T, Nozaki H, Tada T, Hirota M, Irie R, Huffman MA, Nishida T, Kaji M & Koshimizu K (1992*b*) Bitter steroid glucosides, vernoniosides A1, A2, and A3 and related B1 from a possible medicinal plant *Vernonia amygdalina*, used by wild chimpanzees. *Tetrahedron* **48**, 625–632.
Jisaka M, Ohigashi H, Takegawa K, Hirota M, Irie R, Huffman MA & Koshimizu K (1993*a*) Steroid glucosides from *Vernonia amygdalina*, a possible chimpanzee medicinal plant. *Phytochemistry* **34**, 409–413.
Jisaka M, Ohigashi H, Takegawa K, Huffman MA & Koshimizu K (1993*b*) Antitumor and antimicrobial activities of bitter sesquiterpene lactones of *Vernonia amygdalina*, a possible medicinal plant used by wild chimpanzees. *Bioscience, Biotechnology and Biochemistry* **57**, 833–834.
Keymer A, Crompton DWT & Sahakian BJ (1983) Parasite induced learned aversion involving Nippostrongylus in rats. *Parasitology* **86**, 455–460.
Kloos H & McCullough FS (1987) Plants with recognized molluscicidal activity. In *Plant Molluscicides*, pp. 45–108 [KE Mott, editor]. New York: John Wiley & Sons Ltd.
Kokwaro JO (1976) *Medicinal Plants of East Africa*. Nairobi, Kenya: General Printers Ltd.
Koshimizu K, Ohigashi H, Huffman MA, Nishida T & Takasaki H (1993) Physiological activities and the active constituents of potentially medicinal plants used by wild chimpanzees of the Mahale Mountains, Tanzania. *International Journal of Primatology* **14**, 345–356.
Kupchan SM, Hemingway RJ, Karim A & Werner D (1969) Tumor inhibitors XLVII. Vernodalin and vernomygdin, two new cytotoxic sesquiterpene lactones from *Vernonia amygdalina* Del. *Journal of Organic Chemistry* **34**, 3908–3911.
Kyriazakis I, Oldham JD, Coop RL & Jackson F (1994) The effect of subclinical intestinal nematode infection on the diet selection of growing sheep. *British Journal of Nutrition* **72**, 665–677.
McCann C (1932) A cure for tapeworm. *Journal of the Bombay Natural History Society* **36**, 282–284.
Messner EJ & Wrangham RW (1996) *In vitro* testing of the biological activity of *Rubia cordifolia* leaves on primate *Strongyloide* species. *Primates* **37**, 105–108.
Moore M (1979) *Medicinal Plants of the Mountain West*. Santa Fe, NM: Museum of New Mexico Press.
Moutsamboté J, Yumoto T, Mitani M, Nishihara T, Suzuki S & Kuroda S (1994) Vegetation and list of plant species identified in the Nouabalé-Ndoki Forest, Congo. *TROPICS* **3**, 277–293.
Muanza DN, Dangala NL & Mpay O (1993) Zairean medicinal plants as diarrhea remedies and their antibacterial activities. *African Study Monographs* **14**, 53–63.
Murakami A, Ohigashi H & Koshimizu K (1994) Possible anti-tumor promoting properties of traditional Thai foods and some of their active constituents. *Asia Pacific Journal of Clinical Nutrition* **3**, 185–191.
Murakami A, Ohigashi H & Koshimizu K (1996) Anti-tumor promotion with food phytochemicals: A strategy for cancer chemoprevention. *Bioscience, Biotechnology and Biochemistry* **60**, 1–8.
Nelson GS (1960) Schistosome infections as zoonoses in Africa. *Transcripts of the Royal Society of Tropical Medicine and Hygiene* **54**, 301–314.
Neuwinger HD (1996) *African Ethnobotany: Chemistry, Pharmacology, Toxicology*. London: Chapman & Hill.

Nfi A, Ndi C, Bayemi PH, Njwe R, Tchoumboue J, Njakoi H, Mopoi, N, Njakoi M & Django S (1999) The anthelmintic efficacy of some indigenous plants in the Northwest province of Cameroon. *Revue D Elevage et de Medecine Veterinaire des Pays Tropicaux* **52**, 103–106.

Nishida T & Uehara S (1983) Natural diet of chimpanzees (*Pan troglodytes schweinfurthii*): Long term record from the Mahale Mountains, Tanzania. *African Study Monographs* **3**, 109–130.

Nyazema NZ (1987) Medicinal plants of wide use in Zimbabwe. In *Medicinal and Poisonous Plants of the Tropics*, pp. 36–43 [AJM Leeuwenburg, compiler]. Wageningen: Pudoc Wageningen.

Ogilvie GH (1929) Bison eating bark. *Journal of the Bombay Natural History Society* **33**, 706–707.

Ohigashi H (1995) Plants used medicinally by primates in the wild and their physiologically active constituents. *Report to the Japanese Ministry of Science, Education and Culture for 1994 Grant-in-Aid for Scientific Research* (No. 06303012). Tokyo: Japanese Ministry of Science, Education and Culture.

Ohigashi H, Huffman MA, Izutsu D, Koshimizu K, Kawanaka M, Sugiyama H, Kirby GC, Warhurst DC, Allen D, Wright CW, Phillipson JD, Timmon-David P, Delmas F, Elias R & Balansard G (1994) Toward the chemical ecology of medicinal plant-use in chimpanzees: The case of *Vernonia amygdalina* Del. A plant used by wild chimpanzees possibly for parasite-related diseases. *Journal of Chemical Ecology* **20**, 541–553.

Ohigashi H, Jisaka M, Takagaki T, Nozaki H, Tada T, Huffman MA, Nishida T, Kaji M & Koshimizu K (1991) Bitter principle and a related steroid glucoside from *Vernonia amygdalina*, a possible medicinal plant for wild chimpanzees. *Agricultural and Biological Chemistry* **55**, 1201–1203.

Ohigashi H, Sakai Y, Yamaguchi K, Umezaki I & Koshimizu K (1992) Possible anti-tumor promoting properties of marine algae and in vitro activity of wakame seaweed extract. *Bioscience, Biotechnology and Biochemistry* **56**, 994–995.

Okunji CO & Iwu MM (1988) Control of schistomsomiasis using Nigerian medicinal molluscicides. *International Journal of Crude Drug Research* **26**, 246–252.

Oloke JK, Kolawole DO & Erhun WO (1988) The antibacterial and antifungal activities of certain components of *Afromomum melegueta* fruits. *Fitoterapia* **LIX**, 384–388.

Page JE, Balza FF, Nishida T & Towers GHN (1992) Biologically active diterpenes from *Aspilia mossambicensis*, a chimpanzee medicinal plant. *Phytochemistry* **31**, 3437–3439.

Page JE, Huffman MA, Smith V & Towers GHN (1997). Chemical basis for medicinal consumption of *Aspilia* (Asteraceae) leaves by chimpanzees: a re-analysis. *Journal of Chemical Ecology* **23**, 2211–2225.

Palgrave KC (1983) *Trees of Southern Africa*. 2nd revised ed. Cape Town, South Africa: Struik Publisher.

Phillips R (1981) *Mushrooms and Other Fungi of Great Britain and Europe*. London: Pan.

Rausch R (1954) Studies on the helminth fauna of Alaska. XXI. Taxonomy, morphological variation, and ecology of *Diphyllobothirium ursi n*. sp. *provis*. on Kodiak Island. *Journal of Parasitology* **40**, 540–563.

Rausch R (1961) Notes on the black bear, *Ursus americanus* Pallas, in Alaska with particular reference to dentition and growth. *Zeitschrift für Saugetierk* **26**, 77–107.

Riesenberg SH (1948) Magic and medicine in Ponape. *Southwest Journal of Anthropology* **4**, 406–429.

Rodriguez E, Aregullin M, Nishida T, Uehara S, Wrangham R, Abramowski Z, Finlayson A & Towers GHN (1985) Thiarubrine A, a bioactive constituent of *Aspilia* (Asteraceae) consumed by wild chimpanzees. *Experientia* **41**, 419–420.

Rodriguez E & Wrangham RW (1993) Zoopharmacognosy: the use of medicinal plants by animals. In *Recent Advances in Phytochemistry*. vol. 27, *Phytochemical Potential of Tropic Plants*, pp. 89–105 [KR Downum, JT Romeo and H. Stafford, editors]. New York: Plenum Press.

Sengputa S (1981) Adaptive significance of the use of margosa leaves in nests of house sparrows *Passer domesticus*. *Emu* **81**, 114–115.

Smolenski SJ, Silinis H & Farnsworth NR (1974) Alkaloid screening. V. *Lloydia* **37**, 506–536.

Sugiyama Y & Koman J (1992) The flora of Bossou: Its utilization by chimpanzees and humans. *African Studies Monographs* **13**, 127–169.

Swain T (1978) Plant-animal coevolution: A synoptic view of the Paleozoic and Mesozoic. In *Biochemical Aspects of Plant and Animal Coevolution. Phytochemical Society of Europe Symposia Series* no. 15, pp. 3–19 [JB Harbourne, editor]. London: Academic Press.

Toft CA, Aeschlimann A & Bolis L (1991) *Parasite-Host Associations; Coexistence or Conflict?* Oxford: Oxford Science Publications.

Toubiana R & Gaudemer A (1967) Structure du vernolide, nouvel ester sesquiterpique isole de *Vernonia colorata* (Structure of vernolide, new sesquiterpene ester isolate of *Vernonia colorata*). *Tetrahedron Letters* **14**, 1333–1336.

Tutin CEG, White LJT, Williamson EA, Fernandez M & McPherson G (1994) List of plant species identified in the northern part of the Lopé Reserve, Gabon. *TROPICS* **3**, 249–276.

Wakelin D (1996) *Immunity to Parasites – How Parasitic Infections are Controlled*. 2nd ed. Cambridge: Cambridge University Press.

Waterman PG (1984) Food acquisition and processing as a function of plant chemistry. In *Food Acquisition and Processing in Primates*, pp. 177–211 [DJ Chivers, BNA Wood and A Bilsborough, editors]. New York: Plenum Press.

Watt JM & Breyer-Brandwinjk MG (1962) *The Medicinal and Poisonous Plants of Southern and East Africa*. Edinburgh: E. and S. Livingstone Ltd.

Wilson E (1962) *Aubrey's Brief Lives*, p. xix [OL Dick, editor]. Ann Arbor, MI: Ann Arbor Paperbacks.

Wink M, Hofer A, Bilfinger M, Englert E, Martin M & Schneider D (1993) Geese and dietary allelochemicals – food palatability and geophagy. *Chemoecology* **4**, 93–107.

Wrangham RW (1995) Relationship of chimpanzee leaf-swallowing to a tapeworm infection. *American Journal of Primatology* **37**, 297–303.

Wrangham RW & Goodall J (1989) Chimpanzee use of medicinal leaves. In *Understanding Chimpanzees*, pp. 22–37 [PG Heltne and LA Marquardt, editors]. Cambridge, MA: Harvard University Press.

Wrangham RW & Nishida T (1983) *Aspilia* spp. leaves: A puzzle in the feeding behavior of wild chimpanzees. *Primates* **24**, 276–282.

Wrangham RM, Rogers ME & Isabirye-Basuta G (1993) Ape food density in the ground layer in Kibale Forest, Uganda. *African Journal of Ecology* **31**, 49–57.

Yumoto T, Yamagiwa J, Mwanza N & Maruhashi T (1994) List of plant species identified in Kahuzi-Biega National Park, Zaire. *TROPICS* **3**, 295–308.