Eating on the Wild Side

THE PHARMACOLOGIC, ECOLOGIC, AND SOCIAL IMPLICATIONS OF USING NONCULTIGENS

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Nonhuman Primate Self-Medication
with Wild Plant Foods

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Primate researchers generally view foraging strategies as a balance between acquiring the proper nutrients and avoiding toxins and digestion inhibitors (Glander 1982; Waterman 1984), but this view of optimal foraging may ignore potential benefits of certain plant secondary compounds. Unlike ethnobotanists studying human diets who often emphasize the "medicinal" aspects of plants rather than the selection of plant material for nutrients (Etkin and Ross 1991), primatologists may concentrate solely on the dynamic interaction between nutrients and secondary compounds as the explanation for primate foraging behavior. If a nonhuman primate can learn to avoid certain plant species or plant parts because ingestion reduces the animal's fitness (Glander 1975, 1978, 1981, 1982; Glander and Rabin 1983; Hladik 1978; McKee 1979; Milton 1979, 1980; Oates 1977; Oates et al. 1977; Wramgham and Waterman 1983), then nonhuman primates may also be able to learn to exploit the tropical forest medicine chest. Scholars familiar with the use of plants as effective drugs by humans worldwide as discussed elsewhere in this volume should not be surprised that nonhuman primates also use the wild plant medicines available to them in the natural pharmacopoeia of tropical forests.

The study of natural drugs and how they affect animals and people that ingest them is known as pharmacognosy. In 1991, Richard Wramgham and Eloy Rodriguez coined the term zoopharmacognosy to describe self-medication by

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animals in general and nonhuman primates in particular. The first zoopharmacognosy symposium, titled "Zoopharmacognosy: Medicinal Plant Use by Wild Apes and Monkeys," was held in February 1992 at the American Association for the Advancement of Science meetings in Chicago.

The natural history literature is filled with anecdotal evidence that vertebrates use plant medicines. Malay elephants, for example, feed on certain legume creepers (*Entada schefferi*) just before walking long distances (Hubback 1941). Indian wild boars selectively dig and eat the roots of pigweed (*Boerhaavia diffusa*), which humans use as an anthelmintic (Janzen 1978). Mexican folklore suggests that pigs eat pomegranate (*Punica granatum*) roots because they contain an alkaloid toxic to tapeworms (Janzen 1978).

Daniel Janzen (1978) may have been the first to suggest that nonhuman primates are self-medicating when he linked the absence of protozoan parasites in Kibale Forest black and white colobus (*Colobus guereza*) and red colobus monkeys (*C. badius*) with their regular ingestion of plant secondary compounds. Only recently, however, have observations of wild chimpanzees (*Pan troglodytes*) provided the first direct evidence of self-medication by nonhuman primates (Huffman and Seifu 1989). Known and presumed cases of self-medication, as well as the use of nonfood plants by primates, involve chimpanzees (*P. troglodytes*), howling monkeys (*Alouatta palliata*), muriqui (*Brachyteles arachnoides*), black and white colobus monkeys (*C. guereza*), and baboons (*Papio anubis* and *P. hamadryas*), among others.

**Chimpanzees and Plant Medicines**

Chimpanzees in both Gombe Stream National Park and the Mahale Mountains National Park (both are located along the eastern shore of Lake Tanganyika in western Tanzania) eat leaves from the genus *Aspilia* in a highly unusual and characteristic manner (Nishida 1990; Wrangham and Nishida 1983). Normally, chimpanzees stuff leaves in their mouths as fast as they can and chew them into small pieces, but in the case of *Aspilia* spp., the Gombe and Mahale chimpanzees take only one or two of the young leaves at a time and roll them between the tongue and cheek before swallowing the leaves whole. The chimpanzees may be using *Aspilia* spp. in the same manner that humans do for stomach disorders (Wrangham and Nishida 1983). Moreover, ingestion of *Aspilia* leaves by chimpanzees in this manner increases during the time of year when the incidence of intestinal nematodes is highest (Nishida 1990). This nonchewing feeding method results in the *Aspilia* leaves passing through the chimpanzee digestive tract intact and appearing whole in the feces.

The curious method of holding *Aspilia* leaves in the mouth could possibly allow the medication to be absorbed through the cheek in a manner analogous
to the administration of certain medications under the tongue or through the skin and mucous membranes, such as nitroglycerine to humans (Newton and Nishida 1994). This explanation by itself is unlikely since chimpanzees would not need to swallow the leaf if buccal administration were the sole purpose.

Chimpanzees on occasion ingest large quantities of *Aspilia* leaves, but when doing so, they always rapidly chew the leaves (Nishida 1990). Chewing subjects any medicinal compounds in the leaves to deactivation through breakdown and digestion in the stomach. Swallowing the leaf whole protects the compound from deactivation in the stomach and delivers it to the small intestines where it can be absorbed.

To test the hypothesis that *Aspilia* leaves contain a medicinal compound, researchers analyzed *Aspilia* leaves and found high concentrations (5 mg/leaf) of the potent antibacterial, antifungal, and antinematodal agent thiarubrine A (Rodriquez et al. 1985). They reported that this compound has a strong antibiotic effect on bacteria such as *Staphylococcus albus*, *Mycobacterium phlei*, *Bacillus subtilis*, and *Streptococcus faecalis* and is toxic to the nematode *Coenorhabditis elegans*.

Another case of apparent self-medication involved a female chimpanzee in the Mahale Mountains that ate the leaves of *Lippia plicata* at a time when observers judged her to be sick (Takasaki and Hunt 1987). The method of eating was similar to that for *Aspilia* spp. in that the chimpanzee took only one leaf at a time and appeared to suck on each leaf several times before swallowing it. A bioassay indicated potent biological activity, and the local Tongwe people use an infusion of leaves crushed and soaked in water to treat stomachaches (Takasaki and Hunt 1987).

Self-medication and recovery by a nonhuman primate are most convincingly linked in the description of a lethargic chimpanzee with dark urine and bowel irregularity that recovered after sucking the bitter juice from young stems of *Vernonia amygdalina* (Huffman and Seifu 1989). Chimpanzees only rarely consume this plant, known as “bitter leaf,” which humans in tropical Africa use as an anthelmintic and antiscorbutic as well as a tonic to treat intestinal upset and appetite loss (Watt and Breyer-Brandwijk 1962). Several sesquiterpene lactones in *V. amygdalina* (vernodalol, vernolide, and hydroxyvernolide) have demonstrated anthelmintic properties (Koshimizu et al. 1994); these same sesquiterpene lactones, the steroid glucosides (vernonioside A1, A2, A3, and B1), and three of their aglycones in *V. amygdalina* have also demonstrated antischistosomal activities (Jisaka et al. 1992).

Researchers first conducted the antischistosomal tests in vitro using *Schistosoma japonicum*. All of the sesquiterpene lactones inhibited movement and egg laying by schistosomes at 200 ppm, but only vernodalin inhibited movement and egg laying at 20 ppm. The aglycones also all inhibited egg laying at 20 ppm.
When tested in mice, however, vernodalin was lethal to the mice when administered at levels clinically effective against the parasite *S. japonicum*, while oral doses of nonlethal levels had no effect on the parasite (Jisaka et al. 1992). Clinical tests of a closely related plant (*V. anthelmintica*) on humans demonstrated the effectiveness of this plant against pinworm, hookworm, and *Giardia lamblia* (Singh et al. 1981). Although observers (Huffman and Seifu 1989) did not determine whether the aforementioned sick chimpanzee was infected by schistosomes, the above results suggest that vernonioside B₁ (and its aglycones) is effective against parasites such as *S. haematobium* and *S. mansoni*, which cause schistosomiasis, one of most problematic infectious diseases throughout Africa (Jisaka et al. 1992).

Analysis of *V. amygdalina* showed that the leaves have high levels of both vernolide and vernonioside B₁, while the pith from fresh stems contains similar amounts of vernonioside B₁ but only small amounts of vernodalin (Jisaka et al. 1992). Thus, the Mahale Mountain chimpanzee may ingest pith from young *V. amygdalina* stems instead of eating the leaves because the leaves, with their high levels of vernodalin, may be toxic to chimpanzees just as vernodalin was toxic to mice; by eating the pith from stems, the sick chimpanzee may have avoided the highly toxic vernodalin while still obtaining a clinically effective dose of vernonioside B₁. Also, research suggests that vernonioside B₁ may be metabolized into the more effective aglycones (Jisaka et al. 1992).

The toxic nature of many natural plant products must be balanced against the benefits of these products. The difference between life or death may be as simple as choosing stems over leaves from the same tree, as demonstrated by the Mahale chimpanzees. Primates apparently have to choose different plant parts as well as different plant species when medicating themselves. The evidence for self-medication by other nonhuman primates is more circumstantial, but an ever-increasing number of observations cannot be explained solely by the animals' nutrient requirements.

**Howling Monkeys and Plant Medicines**

During the past 22 years I have examined the teeth of more than 950 mantled howling monkeys (*Alouatta palliata*) and have found no cavities or gum disease. However, cavities and severe gum disease afflict chimpanzees (Kilgore 1989). This difference could be related to diet, since the diet of howlers consists mainly of leaves with occasional high levels of sugars from fruits and flowers (Glander 1981), while the diet of chimpanzees consists primarily of sugary fruit (Ghiglieri 1984).

Sugars provide an ideal environment for the bacteria that cause tooth decay. Since oral diseases caused by bacteria such as *Streptococcus mutans* are a serious

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problem for humans (Hamada and Slade 1980), the lack of oral diseases in howlers may be due to the incidence in their diet of plant parts (pedicels) from the cashew (Anacardium occidentale, of the family Anacardiaceae, which also includes poison ivy). These pedicels contain the phenolic compounds anacardic acid and cardol, which exhibit a narrow spectrum of activity against gram-positive bacteria such as Streptococcus mutans that cause tooth decay (Himejima and Kubo 1991).

Internal parasites are common in A. palliata, and it is not unusual to find 100% of the individual monkeys infested (Kuntz and Myers 1972; Stuart et al. 1990). Yet a comparison of populations in two different areas of Costa Rica (Hacienda La Pacifica and Santa Rosa National Park) has demonstrated significant differences in parasite loads: the La Pacifica howlers are heavily parasitized, while the Santa Rosa howlers and spider monkeys carry light parasite loads (Stuart et al. 1990). A major difference between these two populations is the availability of Ficus spp. None of the infected La Pacifica howlers has access to fig trees, while the Santa Rosa howlers have many fig trees available. Many human populations use the latex in Ficus spp. as an anthelminthic (Hansson et al. 1986; Lewis and Elvin-Lewis 1977), and consumption of fig leaves or fruit by the Santa Rosa primates may be keeping their worm load under control.

Twenty-two years of birth records suggest that some female mantled howlers in my study groups may be using plants to influence the sex of their offspring. While the normal sex ratio for the whole La Pacifica population is 1:1, one female had 4 of 4 male infants, another had at least 8 of 9 male infants (the sex of 1 infant was unknown); a third female had 4 of 5 female infants (1 unknown). In each case this represented the total number of infants that each of these females had during her life. These very skewed ratios suggest some extrinsic influence beyond mere chance, particularly when viewed in relation to other documented observations. For example, researchers have reported that naturally occurring phenolic plant compounds influenced reproduction in voles (Microtus montanus) and have suggested that these animals were using the plant chemicals to turn their reproduction on and off (Berger et al. 1977). A follow-up study verified that the plant chemicals acted as the ultimate cue to trigger reproductive effort in M. montanus (Berger et al. 1981).

I do not know the method of preselection being used by howler females, if they are indeed actively influencing the sex of their offspring, but the chemical composition of foods may be cuing the howler’s reproductive efforts in a manner similar to what occurs in voles. The chemical components of food may also offer the female howler an opportunity to affect the sex of her offspring by controlling access of either X or Y sperm to the mature ovum that is shed into the oviduct. Because sperm carrying X or Y chromosomes can be distinguished as, respectively, electropositive and electronegative (Bhattacharya et al. 1979),

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researchers have successfully been able to separate X and Y chromosome-bearing human spermatozoa by electrophoresis (Sevinc 1968). If a female howler were able to produce an electrical charge and change it from positive to negative, she could control whether X or Y chromosome-bearing sperm passed her cervix and entered her uterus to fertilize ova in the oviduct.

To test this hypothesis, I measured the electrical potential at the entrance of the vagina and at the cervix of Costa Rican mantled howlers. The results grouped into two types: those individuals for whom the millivolt reading at the cervix ($\bar{x} = 9.7, N = 36$) was lower than the millivolt reading at the entrance of the vagina ($\bar{x} = 32.5, N = 36$); and those for whom the reading at the cervix ($\bar{x} = 24.4, N = 22$) was higher than the reading at the entrance of the vagina ($\bar{x} = 11.2, N = 22$). In both groups the readings at these two locations were significantly different ($F = 14.72, p = .0004$ and $F = 5.49, p = .024$). Several females also demonstrated a change from positive to negative in readings taken at different times during their reproductive cycles.

Since plant-produced chemicals can trigger the reproductive efforts of mammals (Berger et al. 1977, 1981), similar plant-produced chemicals could possibly change ion concentration in the vagina and affect gender determination. This might be accomplished by ingesting plant compounds that either block or increase the release of calcium, potassium, or sodium through the cell wall in the same manner that phytosterogens either block or facilitate the release of follicle-stimulating hormone or luteinizing hormone in mammals (Hughes 1988; Labov 1977).

_Muriquis and Plant Medicines_

One of the world's rarest primates, the muriqui (*Brachyteles arachnoides*), may be using its forest pharmacopoeia to both reduce parasites and control fertility. In Brazil, perhaps as few as 500 individual muriquis are located in 12 isolated forests (Strier 1992, 1993). With the onset of the rainy season, the muriquis alter their feeding behavior by eating predominantly the leaves of two tree species in the legume family, *Apuleia leiocarpa* and *Platypodium elegans* (Strier 1993). The leaves of these legumes contain compounds that have antimicrobial activity as well as isoflavonoids similar in structure to estrogens. At the beginning of the rainy season, the muriquis make a special effort to eat the fruit of *Enterolobium contortisiliquum*, monkey ear (Strier 1993). This eating pattern may exhibit not a nutritional but a pharmacological perspective, since stigmasterol (a steroid used to synthesize progesterone and found in the monkey ear fruit) may influence the timing of fertility in muriqui (Strier 1993). The stigmasterol could function in the manner of the naturally occurring plant compounds that influence reproduction in voles (Berger et al. 1981).
Most primates carry intestinal parasites, but among four sampled populations in one study an anomalous group of muriquis were completely free of parasites (Stuart et al. 1993). Whereas parasites normally are highest in primate populations exhibiting high density and living in the most disturbed habitats, in this case the parasite-free muriqui lived in a moderately disturbed habitat at the second highest density, while muriqui from the least disturbed and lowest density population had the most parasites. Another unusual finding is that the brown howling monkeys (*A. fusca*) living at the same site as the parasite-free muriquis also did not have any parasites (Stuart et al. 1993). A relationship may hold between this parasite-free condition of the howlers and muriquis and the food they eat (Strier 1992, 1993), since the monkeys appear to ingest some of the same plant material that the Amazonian people eat to treat intestinal worms (Strier 1992). These findings reinforce the potential importance of natural plant products and may prove to be another case of self-treatment by monkeys.

*Colobus and Plant Medicines*

Several feeding behaviors of colobus monkeys cannot be explained solely in terms of nutrient needs and may fit the idea of self-medication. The preferred foods (young leaves) of black and white colobus (*C. guereza*) contain lower amounts of tannin and higher amounts of protein than mature leaves that are not eaten (Oates et al. 1977). The leaves of tree species with high concentrations of tannins are never eaten by black and white colobus but are occasionally eaten by red colobus, *C. badius* (Oates et al. 1977). The same pattern occurs in other primates. For example, mantled howling monkeys usually select leaves that have fairly high levels of protein but little or no tannin (Glander 1981; Milton 1979), but occasionally these same howlers eat leaves with relatively high levels of tannin and phenolics. Plant secondary compounds such as tannin could be beneficial, counteracting bloat and helping to detoxify alkaloids by precipitation (Oates 1977). Whereas most primatologists have been reluctant to accept this self-medication explanation, they have been unable to offer other cogent explanations for the occasional ingestion of tannin-rich plant material by primates such as red colobus and howlers.

Another unusual and controversial behavior is the ingestion of soil by some primates. Arboreal primates are seldom found on the ground, but black and white colobus have been observed on the ground eating clay (Oates 1978). Clay is relatively high in kaolins, and the clay may be ingested to adsorb plant toxins or to adjust the pH of the stomach (Oates 1978). These cases of clay feeding cannot be explained in terms of nutrient gain, but they may be examples of self-medication that find close parallels in the medical cultures and special diets of
many contemporary human groups who avail themselves of the adsorbent and other qualities of clay (Johns and Duquette 1991).

**Baboons and Plant Medicines**

The occurrence of schistosomiasis in baboons (*P. anubis* and *P. hamadryas*) near Awash Falls in Ethiopia may be decreased through the ingestion of *Balanites aegyptiaca* (Phillips-Conroy 1986). The fruit and leaves of this plant are eaten by baboons living below the falls but not by those living above, even though *B. aegyptiaca* occurs evenly distributed in both areas. Both the berries and the leaves contain the steroidal saponin diosgenin, which is active against *Schistosoma* cercariae. Snails surveyed above the falls were negative for schistosomes, while those below tested positive during the dry season. This feeding pattern may offset a higher risk for schistosomiasis in the baboons living below the falls that are more likely to come into contact with schistosome-carrying snails (Phillips-Conroy 1986). In effect, the baboons below the falls ingest plant material that protects them against a virulent parasite.

A follow-up study tested the hypothesis that diosgenin alters the host's hormonal milieu, which produces a less hospitable environment for the adult schistosomes (Phillips-Conroy and Knopf 1986). The study, conducted with mice, revealed that the disease actually increases in mice fed diosgenin. Thus, the hypothesis was not supported, but what is true for mice may not be true for baboons. The researchers in this study argue that generalizations cannot be made about a parasite when different hosts are involved and further suggest that the feeding behavior, ecology, and parasite load of primate species are indeed related (Phillips-Conroy and Knopf 1986).

**The Implications of Nonhuman Primate Self-Medication**

Although much of the documentation for primate self-medication remains anecdotal and circumstantial, good evidence indicates that chimpanzees may be using drugs from their forest medicine chest to treat themselves. This possibility has major implications. Primatologists generally perceive primate foraging strategy as a balance between obtaining sufficient nutrients and avoiding toxins and digestion inhibitors (Glander 1982; Waterman 1984). Except for recent interest, investigators have largely ignored the potential beneficial aspects of plant-produced secondary compounds, which may be the missing link in understanding the connection between primate foraging and social organization. Tropical forests present a complex mix of nutrients, toxins, and medicines. Does each chimpanzee, howler, muriqui, colobus, and baboon have to
learn for itself the difference between food, medicine, and toxin? Or does each learn from older members of the social group?

The answers to these questions will provide important insights for primate social organization and have significant ramifications for understanding human evolution. The ubiquitous occurrence of toxic plant chemicals probably restricted our ancestors’ use of plant products for food, and early humans were unable to use most plant material for food until the development of fire (Leopold and Ardrey 1972; Stahl 1984). In a similar manner, plant-based contraceptives and abortifacients almost certainly affected early humans, who could have been aware of and could have exploited these effects. Certainly, archaeological evidence and written records indicate that ancient and medieval people used plant products to control population size (Riddle and Estes 1992).

The rapid disappearance of forests, which exhibit a diversity of species, means that researchers have little time remaining to determine the effects of plant-produced chemicals on animal and human fertility. Earlier reports that fertility was sharply reduced when sheep fed on one species of clover, *Trifolium subterraneum* (Pope et al. 1960), and that Thai women used an extract from the root of *Pueraria mirifica* (a close relative of kudzu) to induce abortion were met with skepticism (Riddle and Estes 1992). However, evidence such as that from the vole study (Berger et al. 1981) strongly suggests that plants supply more than nutrients. We know that not everything that is green is food, and the nature of the complexity of plant chemicals requires skill and sophistication on the part of plant-eating primates (including humans) to survive.

Another benefit of understanding the primate’s natural pharmacopoeia is the potential discovery of new medicines for human and veterinary use. Many modern drugs including aspirin, morphine, and penicillin can be traced directly to plant origins. Yet researchers have chemically analyzed only a very small percentage of the 250,000 flowering plants in the world (Farnsworth 1993). Investigators cannot test every one of those plants for pharmacologic potential, but we can utilize nonhuman primates to screen them for us. We should not ignore the possibility that our nonhuman primate relatives may provide us with clues for the development of potent new drugs. This possibility also emphasizes the importance of preserving the tropical forests of the world as potential future sources of human medicines.

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