Chapter 12
Medicinal Properties in the Diet of Tibetan Macaques at Mt. Huangshan: A Case for Self-Medication

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12.1 Introduction

Life history strategies include growth, maintenance, and reproduction (Gadgil and Bossert 1970), all of which are dependent upon a proper diet for metabolic functions. Animal feeding strategies are based on finding and consuming a balance of the most essential nutritional elements, carbohydrates, fats, proteins, trace elements, and vitamins, while at the same time avoiding the negative impacts of secondary metabolites in plants (Lambert 2011; Simpson et al. 2004). These secondary metabolites protect plants from predation by an array of insect and vertebrate herbivores that prey upon them by reducing palatability and digestibility (Freeland and Janzen 1974; Glander 1982; Rosenthal and Berenbaum 1992). Nonetheless, this does not always inhibit animals from ingesting such plants in tolerable amounts for purposes other than nutrition.

The idea that animals may ingest plants for their medicinal value was first suggested by Janzen (1978), based on a variety of anecdotal reports from the wild. The study of primate self-medication then began in earnest as a scientific discipline in the mid-to-late 1980s with observations of chimpanzees in the wild (see Huffman 2015). Nonetheless, it is widely documented that humans have traditionally seen animals as a source of knowledge about the use of plants for their medicinal value

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(Engel 2002; Huffman 1997, 2002, 2007). Humans can learn from watching sick wild primates, because we share the same evolutionary history, possess a common physiology, and have lived together under similar environmental conditions for much of our species' history. It has been argued that we have inherited many of the same ways to combat common diseases in the environment (Huffman 2016). Indeed, recent archeological and biochemical evidence supports the idea by showing that one of our closest extinct ancestors, *Homo neanderthalensis*, also used medicinal plants still widely in use today by modern humans (Hardy et al. 2012, 2013; Huffman 2016).

Self-medication research focuses on understanding how animals respond to illness and how these behaviors can be transmitted across generations (Huffman 1997). It has also been argued to be a bio-rational for the exploration and exploitation of novel secondary plant compounds and new insights into how they can be used for the management of health in humans and livestock (Huffman et al. 1998; Krief et al. 2005; Petroni et al. 2016). At the proximate level, self-medication may be driven by the necessity to maintain physiological homeostasis to stay in relatively good condition (Foitova et al. 2009; Forbey et al. 2009).

Currently, the majority of evidence for self-medication in animals comes from the study of how they deal with parasite or pathogen-induced illness (see Huffman 1997, 2011). While some parasitic infections likely go unnoticed, when homeostasis is disrupted or threatened, it is expected to be in the best interest of the host to actively respond in ways to alleviate discomfort. However, there is no reason why self-medication should be limited to parasitosis, since animals are faced with a wide variety of health homeostatic challenges brought upon by such factors as reproductive events, climatic extremes, or other seasonal events (Carrai et al. 2003; Huffman 1997, 2011; Ndagurwa 2012). The ability of a species to defend itself against life-threatening conditions provides a significant adaptive advantage and thus should be present throughout the entire animal kingdom.

In 1997, the concept of "medicinal foods" was formally introduced to primatology, adding the extra element of passive prevention of disease based on the presence of plants in the diet that contain noticeable bioactive, physiology-modifying properties, from which the animals ingesting them could potentially benefit (Huffman 1997). This term was borrowed from the human ethnopharmacological literature (Etkin 1996). For example, among the Hausa of Nigeria, 30% of the wild plant food species they ingest are also used as medicine. Interestingly, of the species used by these people to treat symptoms of malaria, 89% are also eaten as food (Etkin and Ross 1983). Many food items eaten by primates and other mammals have also been shown to contain a variety of secondary metabolites with medicinal properties (roughly 15–25% of any population's food plant species list), suggesting that animals may benefit from the periodic ingestion, in small amounts of these plants (sifaka *Propithecus verreauxi verreauxi*, Carrai et al. 2003; gorillas *Gorilla gorilla* and *G. beringei*, Cousins and Huffman 2002; chimpanzees *Pan troglodytes*, Huffman 1997, 2003; Japanese macaques *Macaca fuscata*, Huffman and MacIntosh 2012; MacIntosh and Huffman 2010; various ungulate species, Mukherjee et al. 2011; lemurs *Eulemur fulvus*, Negre et al. 2006; wooly spider monkeys *Brachyteles arachnoides*, Petroni et al. 2016). The secondary compound rich content of some foods in the diet may play a significant role in the maintenance of health. Two examples associated with risks to parasite infection illustrate this point.

The medicinal diet of chimpanzees in the Mahale M group of Tanzania was examined (Huffman 1998) by conducting a database search using the African ethnomedicine literature. From 172 chimpanzee food species, 43 (22%) items were found to be used to treat parasitic- or gastrointestinal-related illnesses by humans. It was also common for some species to have multiple ethnomedicinal uses. While not all 43 species may have been ingested by chimpanzees in such a way as to benefit from these potential medicinal properties, 33% (20/63) of the plant parts ingested (leaf and stem = 75%, bark 15%, seed = 5%, fruit = 5%) from 16 of these species corresponded to the parts utilized by humans specifically for the treatment of intestinal parasites and gastrointestinal illness.

The medicinal diet and parasite richness of ten Japanese macaque troops were examined (MacIntosh and Huffman 2010). The study troops were selected to represent the species entire distribution, ranging from the extreme cold temperate zone of Shimokita peninsula down to the subtropical island of Yakushima. A total of 1664 plant part items (range, 56–408) from 694 species were the target of an extensive literature search for potential antiparasitic activity in the diet. Of all these ingested items, 198 (from 135 species) were found to have reported antiparasitic properties. The proportion of these antiparasitic items ranged from 12 to 18% across these ten troops. A further 167 plant items (133 species) exhibited medicinal properties not related to parasitic infection or gastrointestinal symptoms. Because nematode species richness is negatively associated with latitude among Japanese macaques (Gotoh 2000), it was predicted that the proportion of antiparasitic items in their diets would also follow the same pattern (MacIntosh and Huffman 2010). A tendency was noted for the proportion of antiparasitic food items to decrease with increasing latitude, and a strong positive statistically significant relationship between the proportions of antiparasitic items ingested and nematode species richness was found. The proportion of medicinal items unrelated to parasite activity showed no such relationship with either latitude or with nematode species richness, supporting the hypothesis that the medicinal diet was somehow influenced by the degree of parasite pressure, relative species richness, and potentially parasite load.

From these and other studies noted above, a pattern is emerging, by which primates and other mammals incorporate certain food items with medicinal properties into their diet. In primates the information thus far shows a strong connection between medicinal food consumption and parasite infection and or reproductive events. Both factors present significant challenges to the survival and fitness of an individual. Knowing what immediate homeostasis challenges that impact individuals of a group can help to better understand how the medicinal components of their diet may work in an animal's favor.

Currently, limited details are available about health and diseases affecting Tibetan macaques (*Macaca thibetana*). In a case study of the troop fission event of YA and YB, the sudden mass death of 17 individuals over a 1-week period was mentioned (Li et al. 1996). Disease was suggested to be responsible, but no diagnosis was given. The speed and widespread effect could be suggestive of an aggressive viral infection, whose virulence was perhaps exacerbated by high stress levels.

Zhu et al. (2012) report the presence of nine intestinal nematode species in Tibetan macaques, with special note of the zoonotic *Gongylonema pulchrum*, having the highest prevalence rate of 31.58%, followed by *Trichuris trichiura* (25.00%), *Oesophagostomum apiostomum* (23.68%), *Ancylostoma duodenale* (hookworm) (14.47%), *Trichostrongylus* sp. (13.16%), and other species of lower prevalence. These parasites are known to be responsible for mild to severe pathogenesis (Brack 1987). Among them, *O. apiostomum* is noted to be responsible for perhaps the severest pathogenesis, in particular among previously infected (pre-immunized) individuals. In these cases, encysted larvae are trapped in the intestinal mucosa by elevated immune response, causing the larvae to die inside the cyst, leading to inflammation, necrosis, and hemorrhaging, and in severe cases leading to secondary bacterial infections, necrosis of the intestinal mucosa, weight loss, weakness, and mortality (Brack 2008). *O. stephanostomum*, a sister species infecting chimpanzees, and other great apes, is equally pathogenic and is associated with self-medicative behaviors used in the therapeutic treatment with *Vernonia amygdalina* by chimpanzees with high-level infections during the rainy season (Huffman 1997; Huffman and Caton 2001). Furthermore, evidence for the possible role of medicinal foods for controlling *O. stephanostomum* and other infections has also been suggested (Huffman 1997).

While more work is clearly needed to understand the different factors affecting the homeostasis of Tibetan macaques (*Macaca thibetana*) possibly leading to self-medication, we take this opportunity to evaluate their diet for its potential medicinal value. We predict there is a proportion of the diet containing plants with medicinal value, and it is our goal to highlight that potential for future research, in order to better understand the role of diet in health maintenance and self-medication in Tibetan macaques.

12.2 Materials and Methods

The subjects of this investigation are Tibetan macaques living in the Valley of the Monkeys (118°11′ W, 30°29′ N), Mt. Huangshan, Anhui Province, China. The site is situated at an elevation of approximately 1840 m above sea level, and the year is divided into four seasons: winter (December to February), spring (March to May), summer (June to August), and autumn (September to November). Average temperatures range from around 0 °C in mid-winter to around 25 °C in summer (Fig. 12.1). Peaks in rainfall occur during the months of May through July, tapering off in autumn and winter. (Further details of the study site are presented in other chapters of this book.)

Analysis of the diet of Yulinkeng 1 (YA1) troop was based on a plant food list previously published by You et al. (2013). At the time of that study, the troop consisted of 28 individuals: 12 adults (4 males, 8 females), 10 juveniles (6 males,

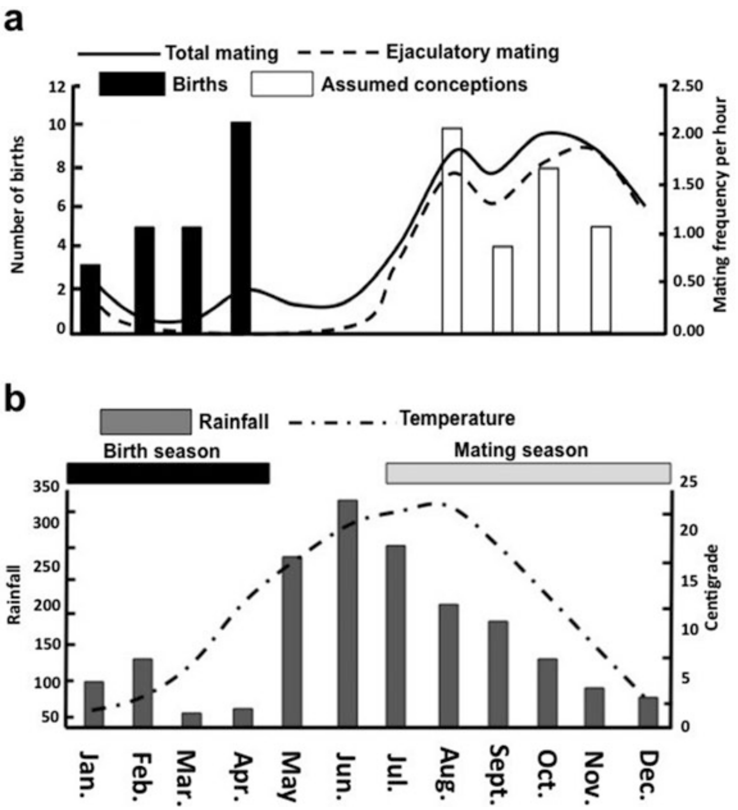

Fig. 12.1 Annual distribution of mating, births, and conceptions of Tibetan macaques (**a**) and monthly rainfall and temperature (**b**) at Mt. Huangshan. These figures were redrawn, modified, and combined from previously published material for illustrative purposes (Li et al. 2005). The meteorological data presented here is the average of 10 years (1983–1992)

4 females), and 6 infants (5 males, 1 female). Direct observations of the troop's feeding behavior in the rugged terrain of Mt. Huangshan are challenging, and to overcome these difficulties, the investigators produced a food list based on the analysis of 81 fecal samples collected over 10-day blocks, one block each during winter, spring, summer, and autumn between November 2011 and October 2012 (You et al. 2013). While the study covered just 1 year, it provides an important basis for an evaluation of the medicinal potential of food items ingested by the troop during that period.

The method used to quantify the relative contribution of each plant species (part) took a microhistopathological approach to identify ingested food remains in the feces. The method is a validated, well-established, procedure developed by Sparks and Malechek (1968) and has been used to quantify the botanical composition of diets in a variety of free-ranging, sometimes difficult to directly monitor, domestic and wild animals in their natural habitats (e.g., mule deer *Odocoileus hemionus*, Anthony and Smith 1974; musk deer *Moschus leucogaster*, Green 1987; domestic goats *Capra aegagrus hircus*, Mellado et al. 1991; cattle *Bos taurus*, sheep *Ovis aries*, Angora goats, Alipayo et al. 1992; wild turkeys *Meleagris gallopavo*, Rumble and Anderson 1993; Yunnan snub-nosed monkeys *Rhinopithecus bieti*).

The method requires the assembly of histopathological plant tissue reference key slides prepared from identified plant species in the habitat. These keys are then used to microscopically identify plant parts in the feces based on each species' unique cell tissue structure characteristics (see Ahmed et al. 2015). At Huangshan, a total of 224 plant species (73 families) in the habitat were identified and histopathological reference keys were made (You et al. 2013). They calculated the relative density (RD) of each species (and family) present in the feces using the following formula, where:

$$\mathrm{RD} = \text{the density of a plant particle}/\text{the total density of all plant particles} \times 100.$$

We evaluated the medicinal properties of each plant species in the resulting list for medicinal value using online database sources [Traditional Chinese Medicinal Plants (Duke and Ayensu 1985); Find Me A Cure (2018); Herbpathy Data Base (2018); Plants For A Future Data Base (1996–2012); World Agroforestry Data Base (2018)], followed up with Google Scholar article searches by plant species and/or active compound name, focusing on the plant items (leave, fruits, stems, bark, roots, flowers) ingested by YA1 troop members.

Data sorting and descriptive statistics were carried out using Microsoft® Excel® for Mac 2011 (Ver. 14.7.2.). Statistical analyses for chi-square were carried out using an online calculator: https://www.socscistatistics.com/tests/chisquare2/Default2.aspx. Statistical significance was set at 0.05.

12.3 Results and Discussion

12.3.1 Plant Food Species and Their Relative Density (RD) Values

To put the medicinal foods ingested by members of the troop into perspective, we first describe the overall trends of their feeding habits as revealed in the dietary analysis. The plant food species consumed by YA1 troop members are listed in descending order of RD by family and species in Table 12.1. The species RD values are summarized seasonally, with each season totaling 100%. Fifty species (61 different items, 26 families) from across the entire study period were analyzed here. Of the 61 items ingested, leaves accounted for 78%, by far the largest proportion of plant parts found, followed by fruits 11%, stems 3%, buds 2%, seeds 2%, young shoots 2%, and flowers 2%.

Table 12.1 Plant food species, part(s) eaten, and seasonal variation of use in the YA1 troop of Tibetan macaques at Mt. Huangshan

Family and species	Parts Consumed	Relative density (RD) Winter	Spring	Summer	Autumn
Fagaceae					
*Castanpopsis eyre*i (Champion ex Bentham) Tutcher	Leaf, fruit	14.78%	9.17%	10.49%	14.48%
Lithocarpus glaber (Thunb.) Nakai	Leaf, fruit	6.60%	6.62%	4.27%	6.46%
Quercus myrsinaefolia Blume	Leaf, fruit	6.06%	7.38%	7.41%	9.37%
Quercus glauca Thunb.	Leaf, fruit	2.50%	3.12%	5.05%	7.69%
Quercus glandulifera Blume	Leaf, fruit	0	1.22%	5.41%	2.08%
Quercus aliena Blume	Leaf, fruit	0	0	0	0.60%
Lauraceae					
Litsea coreana H. Léveillé	Leaf	12.09%	8.08%	9.55%	4.66%
Machilus leptophylla Handel-Mazzetti	Leaf	4.53%	2.53%	6.84%	7.11%
Phoebe sheareri (Hemsley) Gamble in Sargent	Leaf	4.04%	2.88%	5.12%	5.55%
Machilus thunbergii Siebold & Zuccarini	Leaf, bud	0.66%	13.50%	2.20%	1.68%
Lindera aggregata (Sims) Kostermans	Leaf	0	0.17%	0.30%	0.07%
Poaceae					
Zea mays L. (corn)	Seed	8.94%	7.13%	6.76%	4.06%
Carex tristachya Thunberg in Murray	Leaf	2.08%	2.82%	4.78%	1.37%
bamboo	Young shoots	3.47%	2.88%	2.65%	2.16%
Ericaceae					
Rhododendron ovatum (Lindley) Planchon ex Maximowicz	Leaf	3.37%	3.97%	1.54%	2.65%
Vaccinium bracteatum Thunberg in Murray	Leaf	2.05%	1.34%	2%	1.06%
Rhododendron sp.	Leaf, flower	1.27%	0.87%	2.07%	1.22%
Vaccinium mandarinorum Diels	Leaf		1.40%	1.30%	0.68%
Hamamelidaceae					
Loropetalum chinense (R. Brown) Oliver	Leaf, stem	5.18%	4.09%	3.51%	2.81%
Distylium myricoides Hemsley	Leaf, stem	1.31%	0.35%	1.26%	1.61%
Liquidambar formosana Hance	Leaf	0	0.23%	0	0
Theaceae					
Camellia cuspidata (Kochs) H. J. Veitch	Leaf	5.18%	4.76%	2.84%	3.81%
Eurya alata Kobuski	Leaf	1.09%	0.64%	1.44%	0.37%
Eurya muricata Dunn	Leaf	0	0.58%	0	1.45%
Eurya nitida Korthals	Leaf	0	0.23%	3.58%	2.08%

(continued)

Table 12.1 (continued)

Family and species	Parts Consumed	Relative density (RD) Winter	Spring	Summer	Autumn
Leguminosae					
Millettia dielsiana Harms. ex Diels.	Leaf	2.36%	2.53%	1.88%	1.84%
Lespedeza bicolor Turczaninow	Leaf	0	0.35%	1.44%	0
Saxifragaceae					
Itea omeiensis C. K. Schneider in Sargent	Leaf	2.09%	1.34%	1.09%	0.22%
Taxaceae					
Torreya grandis Fortune ex Lindley	Leaf	1.37%	0.64%	0	0
Aquifoliaceae					
Ilex purpurea Hassk.	Leaf	0.52%	0.29%		0.68%
Myrtaceae					
Syzygium buxifolium Hooker & Arnott	Leaf	0.49%	0.06%	0.75%	0.15%
Cephalotaxaceae					
Cephalotaxus fortunei Hooker	Leaf	0.40%	0	0	0
Taxodiaceae					
Cunninghamia lanceolata (Lambert) Hooker	Leaf, fruit	7.60%	0.11%	0.91%	2.08%
Ranunculaceae					
Thalictrum aquilegifolium L.	Leaf	0	0.11%	0.53%	0
Anacardiaceae					
Toxicodenddron sylvestre (Siebold & Zucc.) Kuntze	Leaf	0	0.17%	0.83%	0.30%
Araliaceae					
Hedera nepalensis var. *sinensis* (Tobler) Rehder	Leaf	0	0.29%	0	1.76%
Styracaceae					
Pterostyrax corymbosus Siebold & Zuccarini	Leaf	0	0.23%	0	0
Tiliaceae					
Tilia oliveri Szyszyłowicz	Leaf	0	0.52%	1.13%	0
Berberidaceae					
Epimedium davidii Franchet	Leaf	0	0.23%	0	0
Gesneriaceae					
Conandron ramondioides Siebold & Zuccarini	Leaf	0	0	0	0.30%

(continued)

Table 12.1 (continued)

Family and species	Parts Consumed	Relative density (RD) Winter	Spring	Summer	Autumn
Araceae		0	1.33%	0	0
Pinellia cordata Dunn.	Leaf	0	0.11%	0	0
Grassleaf Sweetfalg	Leaf	0	1.22%	0	0
Lardizabalaceae		0	0.46%	0	2.05%
Akebia trifoliata (Thunberg) Koidzumi	Leaf	0	0.06%	0	0.83%
Akebia quinata (Houttuyn) Decaisne	Leaf	0	0.23%	0	1.22%
Sargentodoxa cuneata (Oliver) Rehder & E. H. Wilson in Sargent	Leaf	0	0.17%	0	0
Rosaceae					
Rhaphiolepis indica (Linnaeus) Lindley	Leaf	0	2.88%	1.07%	1.92%
Photinia davidsoniae Hook.	Leaf	0	0.58%	0	0.15%
Cucurbitaceae					
Thladiantha nudiflora Hemsley	Leaf	0	0.46%	0	0
Actinidiaceae					
Actinidia lanceolata Dunn.	Leaf	0	0	0	3.47%
Menispermaceae					
Menispermum dauricum Candolle	Leaf	0	1.40%	0	0
Food species consumed		18	35	25	30
Medicinal food species consumed		7	11	6	7

List is modified from You et al. (2013). RD percentages are summarized per season. $n = 50$ species
Medicinal food species consumed are highlighted in grey

Seasonal variation was noted in the number of plant species ingested from their total repertoire (Fig. 12.2), but these differences were not statistically significant ($\chi^2 = 6.93$, $df = 3$, $p > 0.05$). The largest number of species consumed was in spring ($n = 46$), followed by autumn ($n = 37$), summer ($n = 31$), and winter ($n = 25$). With the exception of one species, *Cunninghamia lanceolata* (Taxodiaceae) whose leaves and fruit were both consumed, all ingested fruit items (nuts, acorns) come from the Fagaceae family. Combined, use of leaf and fruit items in this family had the highest RD values of all plant food species identified, and none of these were classified as medicinal foods. The highest of these RD values were recorded in autumn and summer and involved the consumption of ripening and fallen ripe fruits, the main food items sought after in these two seasons. The second largest RD value family was Lauraceae, with five species, whose leaves and buds were consumed. Only one of the five species in this family, *Litsea coreana,* was classified as a medicinal food.

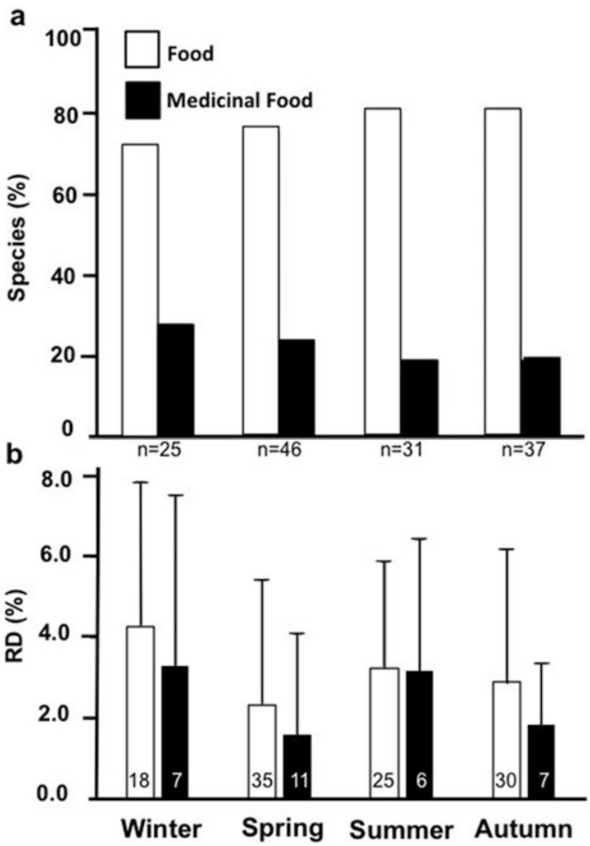

Fig. 12.2 Seasonal variation in the ingestion of food and medicinal food species (**a**) and average RD values of food and medicinal food species by YA1 troop. (**b**) Mean RD values calculated from individual species RD values per season presented in Table 12.1. Data derived from You et al. (2013)

12.3.2 Medicinal Foods in the Diet

Across the entire study period, 12 species (13 items: 12 leaves, 1 stem) in the diet had notable medicinal activity in the plant part ingested by members of YA1 troop (Table 12.1). Our literature search revealed an array of pharmacological properties of high medicinal value including antiparasitic, antiprotozoal, antibacterial, antifungal, antiviral, anti-dysentery, anti-enteritis, anticancer (antitumor), anti-inflammation, antirheumatic, antidiabetic, cardiovascular protective, neuroprotective, osteoprotective, reproductive stimulant, antidepressant, immunosuppressant, and diaphoretic; treatment for ulcers, wounds, skin disease, weakness, and dizziness; and other health-protecting and health-promoting activities. Associated with these activities are a variety of physiologically active secondary plant metabolites (Appendix).

The following are detailed descriptions of the 12 plant species' seasonality of use, life form, pharmacological properties, and prescribed uses by humans.

***Cephalotaxus fortunei* (Leaf, Used in Winter) Evergreen Tree** Abietane diterpenoids synthesized by suspension-cultured cells displayed a wide spectrum of biological activities including antiparasitic, antibacterial, antifungal, and antiviral properties. These compounds were found to be effective against pathogens such as *Mycobacterium tuberculosis* and *Staphylococcus aureus*, including methicillin-resistant (MRSA) strains and biofilm infection of *S. aureus* (Neto et al. 2015). Abietane diterpenes isolated from aerial parts of *Plectranthus barbatus* showed remarkable activity with acceptable selectivity against the blood parasites *Plasmodium falciparum* (malaria) and *Trypanosoma brucei* (sleeping sickness in animals). Nonspecific antiprotozoal activity was also detected and is likely due to the compound's high cytotoxicity (Mothana et al. 2014). This plant also demonstrates significant anticancer activity (Duke and Ayensu 1985).

***Epimedium davidii* (Leaf Used in Spring) Perennial Herb** Compounds isolated from the leaves include Icariside II (Baohuoside I) and Baohuoside II, III, V, and VI (Ma et al. 2011). These compounds possess therapeutic activities such as osteoprotective effect, neuroprotective effect, cardiovascular protective effect, anticancer effect, anti-inflammation effect, immunoprotective effect, and enhancement of reproductive function (sexual health for males and females) (Li et al. 2015). Treatment with the compound icariin is reported to significantly increase epididymal sperm counts and testosterone levels of male rats (Chen et al. 2014) and significantly increases erectile function in castrated Wistar rats by increasing the percentage of smooth muscle and inducible nitric oxide synthase in the corpus cavernosum (Liu et al. 2005). Active ingredients administered at a dose of 5 g/kg^{-1} with an ig volume of 5 mL kg^{-1} alleviated the impact of high-intensity exercise on serum testosterone, maintaining it at normal physiological levels. It can also promote protein synthesis, inhibit degradation of amino acid and protein, and increase hemoglobin and glycogen reserves in rats receiving exercise training (Zhou et al. 2013).

A series of tests on rats and mice using icariin have also reported significant stress reduction and antidepressant properties via downregulation of glucocorticoid receptor activity and regulation of hippocampal neuroinflammation are associated with this plant species (Pan et al. 2010; Wu et al. 2011; Gong et al. 2016). The leaves of this species are also noted for their anticancer activity (Frohne and Pfänder 1984), immunosuppressive action, and inhibitory properties of lymphocyte activation (Ma et al. 2004).

***Hedera nepalensis* (Leaf Used in Spring and Autumn), Evergreen Climber or Creeper Vine** The leaves and berries are reported to have cathartic, diaphoretic, and stimulant properties. A decoction is used to treat skin diseases. Significant cancer chemo-preventative and cytotoxic properties have been demonstrated (Jafri et al. 2016). It is also reported to be an important folk medicine for the treatment of diabetes. No specific mention of *H. nepalensis* is given, but a closely related species *Hedera helix* is relevant to this discussion, as it has a similar chemical makeup and has been noted to be poisonous in large doses, but the leaves are eaten without observed side effects in wild mammals. Leaves contain hederagenin, a saponic glycoside, which can cause gastrointestinal nervous system disturbances, breathing difficulties, and coma if eaten in large amounts (Plants For A Future.com).

***Ilex purpurea* (Leaf Used in Winter, Spring, and Autumn) Evergreen Tree** The plant is considered to be one of the 50 fundamental herbs in Chinese medicine. It is reported to have antitumor properties, and an extract of the leaves is made into a solution and used for treating burns and ulcers in the lower extremities. The ashes of burnt leaves are used as a dressing for skin ailments and infected wounds (Duke and Ayensu 1985).

***Lespedeza bicolor* (Leaf Used in Spring and Summer) Deciduous Shrub** Leaves contain flavonoids, alkaloids, terpenes, organic acids, and stigmasterols. Potential for antioxidant, anticancer, and antibacterial activity is also noted (Ullah 2017) and is traditionally used for coughs and colds, kidney and urethra problems, fever, headache, weakness, and dizziness (Chang et al. 2017).

***Liquidambar formosana* (Leaf Used in Spring) Deciduous Tree** The leaves are used in the treatment of cancerous growths (Duke and Ayensu 1985).

***Litsea coreana* (Leaf Used Year Round) Evergreen Tree** Exhibits notable bioactivities, such as hepatoprotection, hyperglycemia, anti-inflammation, antioxidation, and antibacterial properties through multiple molecular mechanisms. These compounds augment immunoglobulin M and G values and show significant inhibitory effects on the pathogens *Bacillus anthracis, Proteusbacillus vulgaris, Staphylococcus aureus*, and *Bacillus subtilis*. Anti-HSV-1 activity and anti-gastric carcinoma and anti-colon carcinoma HT-29 activity have been reported. Leaves contain polysaccharides, polyphenols, essential oils, and numerous flavonoids (Jia et al. 2017).

***Loropetalum chinense* (Leaf, Stem Used Year Round) Evergreen Woody Shrub** The leaves are crushed and pulverized for external application on wounds (Find Me A Cure.com), while a decoction of the whole plant is used to treat coughing in tuberculosis patients and is a treatment against dysentery and enteritis. This species also promotes wound healing and possesses antibacterial, anti-inflammatory, antioxidant, and antitumoral activity, as well as adjusts fat metabolism, and protects from cardiovascular disease (Zhou et al. 2014).

***Millettia dielsiana* (Leaf Used Year Round) Deciduous Shrub** A decoction or tincture of leaves is used to treat hookworm, roundworm (nematodes), and filarial infections and is a treatment for amenorrhea, metrorrhagia, anemia, traumatic injuries, and rheumatoid arthritis (Anonymous 1977; Yeung 1985). Stem extracts exhibit anti-enterovirus activity and is effective against Coxsackie virus B3, Coxsackie virus B5, Poliovirus I, Echovirus 9, and Echovirus 29 (Guo et al. 2006). It also aids in the prevention of cardiovascular and cerebrovascular disease. It possesses high antioxidant activity (Gan et al. 2010). Seven isoflavones have been isolated from the stem and identified as 6-ethoxyca lpogonium isoflavone A, durmillone, ichthynone, jamaicin, toxicaro l isoflavone, barbigerone, and genistein (Gong et al. 2007).

***Sargentodoxa cuneata* (Leaf Used in Spring) Deciduous Climbing Shrub** The stem is anthelmintic, antibacterial, antirheumatic, carminative, diuretic, and tonic (Usher 1974; Anonymous 1977; Yeung 1985; Duke and Ayensu 1985). The mashed leaves are plastered onto sores (Duke and Ayensu 1985). A decoction or tincture is used in the treatment of anemia, traumatic injuries, rheumatoid arthritis, hookworm disease, roundworm, and filariasis (Anonymous 1977; Yeung 1985). Stem extracts exhibited anti-enterovirus activity against anti-Coxsackie virus B3, Coxsackie virus B5, Polio virus I, Echovirus 9, and Echovirus 29 (Guo et al. 2006).

***Syzygium buxifolium* (Leaf Used Year Round) Evergreen Shrub** The juice of macerated leaves are taken to reduce fever (Duke and Ayensu 1985). Leaf powder is rubbed on the skin of smallpox patients for its cooling effect (World Agroforestry.org).

***Vaccinium bracteatum* (Leaf Used Year Round) Evergreen Shrub** Leaves contain isoorientin, orientin, vitexin, isovitexin, isoquercitrin, quercetin-3-O-α-L-rhamnoside, and chrysoeriol-7-O-β-D-glucopyranoside. Radical scavenging activity and protection against KBrO3-mediated kidney damage have been demonstrated (Zhang et al. 2014a, b). Anticancer and anti-inflammatory activity was demonstrated (Landa et al. 2014).

12.3.3 Seasonality of Medicinal Food Ingestion

In total, 76% of the 50 species (61 food items from 26 families) reported in YA1 troop's diet showed no evidence of significant toxicity or pharmacological activity, supporting the assumption that most plants in the diet are indeed selected for their nutritional value. However, the remaining 24% ($n = 12$) of the species are considered medicinal foods, with potential health-promoting properties.

There was no statistically significant seasonal difference in the number of medicinal foods in the diet ($\chi^2 = 0.9371$, $p > 0.05$, $df = 3$; Fig. 12.2). However, more medicinal food species were consumed in winter (28%) and spring (24%) and then summer (19%) or autumn (19%). All the consumed medicinal plant items were leaves. Seven of these species are evergreen trees, shrubs, or creepers, so leaves of these species are available year-round. The remaining five species were deciduous trees or shrubs, with leaves only in spring and summer months. These results suggest a broad based potential for access to medicinal food across the year. While the number of potential medicinal species ingested is not significantly different across seasons, the particular species ingested varied between seasons in some cases and present some interesting patterns related to their possible seasonal benefits. The three following categories of health concern extracted from our analysis provide some important areas for future investigation.

12.3.4 Antiparasitic Properties

Previous reports of medicinal food ingestion and therapeutic self-medication in response to parasite infections point out the relationship between seasonality of reinfection and plant ingestion as evidence for the context of plant use (Huffman et al. 1997, 1998). While no clear-cut seasonal trend for medicinal food ingestion was apparent in the YA1 troop diet, the relationship between medicinal properties of five specific medicinal food species and their seasonality of use provides information for future detailed investigation. *C. fortunei, L. bicolor, L. coreana, L. chinese,* and *S. cuneata* are reported to possess significant broad-spectrum antiparasitic, antibacterial, and antiviral activity. One of the highest RD values of all medicinal foods was assigned to *L. coreana* (RD = 12.09%) consumption in winter. However, two of the most intriguing medicinal food candidates with wide-spectrum antiparasitic properties are *C. fortunei* and *S. cuneat*a, even though both had low RD values (0.40 and 0.17, respectively). Ingestion was restricted to winter in the former and spring in the later.

Winter and spring, the mating and birth seasons, respectively, could be potentially key seasons for investigating the parasite infection status of individuals before and after the ingestion of these plant species. One of the three zoonotic parasites identified in YA1 troop is *O. apiostomum* (Zhu et al. 2012). Infection in Japanese macaques by *O. apiostomum* occurs more frequently during winter months (MacIntosh et al. 2010), and self-medication in response to a sister species, *O. stephanostomum*, occurs in chimpanzees (Huffman 1997). The reduction of worm burden and temporary relief from related gastrointestinal upset has been linked to the ingestion of the bitter pith of *V. amygdalina* (Huffman et al. 1993, 1996a). In vitro pharmacological assays of *V. amygdalina* demonstrate a broad range of antiparasitic activities (e.g., Ohigashi et al. 1994; Oyeyemi et al. 2018).

For respiratory viruses, seasonal changes in humidity improve viral survival and increase opportunities for infection (Altizer et al. 2006). A general survey of disease prevalence in YA1 troop is necessary to provide further insights about the ecology of infection dynamics that could lead to important links with their medicinal diet. *L. bicolor* is associated with possible respiratory health, and a number of other species could inhibit respiratory viruses from establishment (Chang et al. 2017).

12.3.5 Reproductive Modulation

Throughout history, humans have utilized a number of plant hormones to suppress or enhance their reproductive and sexual activity (Lewis and Elvin-Lewis 1977). The reproductive behavior of male and female Tibetan macaques has been studied from a variety of perspectives including endocrinology, behavior, and seasonal variation (e.g., Li et al. 2005; Xia et al. 2018; Zhao 1993). Tibetan macaques at Mt. Huangshan exhibit high levels of sexuality inside and sometimes outside of the mating season (Li et al. 2007, see Fig. 12.2 above; Xia et al. 2010). Could there be something in the diet that stimulates or enhances Tibetan macaque sexual behavior?

One medicinal food consumed by YA1 troop in particular deserves attention in this respect. Used as an aphrodisiac in Chinese traditional medicine, *E. davidii* is known as horny goat weed or rowdy lamb herb (Ma et al. 2011), suggesting an origin for the use of this plant from watching the behavior of animals. Experimental studies have demonstrated significant enhancement of reproductive function, including increased sperm count, testosterone levels, and enhanced erectile function in rats (Chen et al. 2014; Li et al. 2015; Liu et al. 2005), but ingestion of *E. davidii* by macaques at Mt. Huangshan is limited to spring, the birth season of this troop. The seasonal timing of the consumption of this plant is preceded by a decline in ejaculatory mating frequency at the end of the mating season in late winter. For a few months in spring, non-ejaculatory mating continues at low levels with a slight peak around April (Fig. 12.1). Could the ingestion of this plant be having some effect on their reproductive activity? There is precedence in the literature to believe there might be.

Ingestion of plant hormones by animals has been found to have a number of other influences on reproductive behavior (e.g., Berger et al. 1977; Starker 1976; Sadlier 1969). Wasserman et al. (2012) report the seasonal influence of estrogenic plant consumption on hormonal and behavioral fluctuations in red colobus monkeys (*Procolobus rufomitratus*) in Uganda. Peaks in the consumption of young leaves (*Millettia dura*) with high estrogen levels coinciding with both fecal estradiol and cortisol levels in the feces. This was associated with increased levels of both copulation and aggressive interactions. In a study by Whitten (1983), the timing of onset, duration, and ending of seasonal mating behavior in female vervet monkeys (*Cercopithecus aethiops*) were closely correlated with the availability and ingestion of the flowers of *Acacia elatior* (Mimosaceae). Later Garey et al. (1992) analyzed the flowers of this species and found them to be estrogenic. Garey and colleagues determined that the amount of flowers consumed by vervet monkeys could provide adequate exogenous estrogen to stimulate the onset of mating activity. *Sargentodoxa cuneata* is only ingested during the spring birth season and has been found to assist in menstrual regulation among people, as a prophylactic against amenorrhea or metrorrhagia (Anonymous 1977; Yeung 1985). Therefore, including this species in the diet could have some sex steroid-like properties that have a role in modifying female reproductive status after birth.

Phytoestrogens present in the diet of many primates have been proposed to affect birth spacing, influence the sex of offspring, and regulate fertility. Glander (1980) proposed that inter-annual variation in birth spacing of howler monkeys (*Alouatta palliata*) was due to inter-annual variation in food quality. That is births were concentrated seasonally in years when secondary compound concentration in plant foods were low (high food quality) and spread across the year when concentrations were high (low food quality).

An in-depth examination of sex and reproduction in the Gombe chimpanzees by Wallis (1995, 1997) noted significant seasonal patterns, and multiple reproductive parameters including conception, anogenital swelling, infant mortality, and fertility. Wallis proposed that intensive foraging on seasonally available plant foods containing phytoestrogens mediate these fertility factor (Wallis 1992, 1994, 1997).

Hence, both male and female Tibetan macaque reproductive biology and behavior might be influenced by the inclusion in the diet of plants that have been shown in other species to influence reproductive hormones.

12.3.6 Stress Reduction

Stress disrupts health homeostasis, affecting reproductive function, overall health, and well-being of animals. Stress can be induced by both environmental and social factors, leading to physiological and behavioral imbalances (e.g., Takeshita et al. 2013, 2014; Wooddell et al. 2016). For example, primates living in seasonally cold habitats have a number of behavioral means for ameliorating cold stress, such as staying warm by sleeping and resting site selection, huddling, and, in one unique case, taking therapeutic hot spring baths (e.g., Hori et al. 1977; Zhang and Watanabe 2007; Kelley et al. 2016; Takeshita et al. 2018).

For stress induced by social interactions relating to social instability, dominance interactions, intergroup encounters, competition for food or mates, etc., affiliative behaviors such as grooming, reconciliation, consolation, and nonreproductive sexual behavior have been reported to be mechanisms of physiological reduction of stress in socially living species. Primates in particular have received wide attention (e.g., Aureli et al. 2002; Berry and Kaufer 2015; Carter et al. 2008; Fraser et al. 2008).

Tibetan macaques are classified as having a despotic, strongly linear, dominance style (Berman et al. 2004). They are well known for their kin-biased affiliation, tolerance, post-conflict reconciliation, nonreproductive mating, and the use of infants as a buffer to reduce tension between adults: "bridging" behavior (e.g., Bauer et al. 2014; Berman et al. 2004, 2007; Li et al. 2007; Ogawa 1995a, b). This suite of behaviors is linked to stress reduction through conflict buffering, suggestive of an undercurrent of social stress in their daily lives. Schenepel (2015) recorded high levels of agonistic and submissive behaviors around the provisioning area of YA1 troop compared to non-provision areas in the forest. Within the context of our study, we pose the question: "Do Tibetan macaques also have a dietary choice that aids in stress reduction?"

E. davidii is a prime candidate. Experimental evidence from several studies on hormonal and behavioral stress amelioration has been reported in relation to the administration of icariin, a major flavonoid isolated from *E. davidii*, in stress-induced rats and mice (Pan et al. 2010; Wu et al. 2011; Liu et al. 2015; Gong et al. 2016). Wu et al. (2011) demonstrated that icariin markedly decreased stress-induced downregulation of glucocorticoid receptors in mice subjected to "social defeat" by conspecifics. The compound also displays antidepressant activity and is used in Chinese traditional medicine for this purpose.

To the best of our knowledge, a dietary strategy for stress reduction has not yet received attention in the animal self-medication literature. Further investigation of the context of stress and the ingestion of plants like *E. davidii* may allow us to expand our knowledge of the role of diet in this area as well (Table 12.2).

Table 12.2 Medicinal properties of the 12 candidate "medicinal foods" in the diet of YA1 troop of Tibetan macaques at Mt. Huangshan

Species (part ingested) [season of use] form	Medicinal properties (see text for references and further details)
Cephalotaxus fortunei (leaf) [winter] evergreen, tree	Antiparasitic antibacterial, antifungal, and antiviral properties. Effective against pathogenic *Mycobacterium tuberculosis* and *Staphylococcus aureus*, including methicillin-resistant (MRSA) strains and biofilm infection of *S. aureus*. Contains abietane diterpenes showing remarkable activity against *Plasmodium falciparum* (malaria), *Trypanosoma brucei* (sleeping sickness in animals). Nonspecific antiprotozoal activity likely due to high cytotoxicity. Cancer prevention properties
Epimedium davidii (leaf) [spring] herbaceous, perennial	Enhancement of reproductive function (erectile, sperm count, testosterone levels). Stress reduction and antidepressant properties via downregulation of glucocorticoid receptor activity and regulation of hippocampal neuroinflammation. Anticancer activity, immunosuppressive action, and inhibition of lymphocyte activation. Osteoprotective effect, neuroprotective effect, cardiovascular protective effect, anti-inflammation effect, and immunoprotective effect
Hedera nepalensis (leaf) [spring, autumn] evergreen climber or creeper vine	Purgative action, sweat-inducing and stimulant properties. Used to treat skin diseases. Cancer preventative and cytotoxic properties. Important folk medicine for the treatment of diabetes. Contains saponins and is toxic. Ingestion induces gastrointestinal nervous system disturbances
Ilex purpurea (leaf) [winter, spring, autumn] evergreen tree	One of the 50 fundamental herbs in Chinese medicine. Antitumor properties. Used for treating burns, ulcers in the lower extremities
Lespedeza bicolor (leaf) [spring, summer] deciduous shrub	Antioxidant, anticancer, and bactericidal activity. Traditionally used for coughs and colds, kidney and urethra problems, fever, headache, weakness, and dizziness. Contains flavonoids, alkaloids, terpenes, organic acids, and stigmasterols
Liquidambar formosana (leaf) [spring] deciduous tree	Treatment of cancerous growths
Litsea coreana (leaf) [year-round] evergreen tree	Augments immunoglobulin M and G values and shows significant inhibitory effects on pathogenic *Bacillus anthracis, Proteusbacillus vulgaris, Staphylococcus aureus*, and *Bacillus subtilis*. Anti-HSV-1 activity, anti-gastric carcinoma and colon carcinoma HT-29 activity. Exhibits antibacterial, hepatoprotective, hyperglycemic, anti-inflammatory, and antioxidation activity. Contains polysaccharides, polyphenols, essential oils, and numerous flavonoids
Loropetalum chinense (leaf, stem) [year-round] evergreen woody shrub	An external application to wounds. A treatment for coughing in patients with tuberculosis, dysentery, and enteritis. Promotes wound healing, possesses antibacterial activity. Anti-inflammatory and antioxidant activity. Adjusts fat metabolism. Contains antitumoral activity and protects from cardiovascular disease

(continued)

Table 12.2 (continued)

Species (part ingested) [season of use] form	Medicinal properties (see text for references and further details)
Millettia dielsiana (leaf) [year-round] deciduous shrub	Used for prevention of cardiovascular and cerebrovascular disease. Significant antioxidant activity
Sargentodoxa cuneata (leaf) [spring] deciduous climbing shrub	Anthelmintic (hookworm, roundworm, filariasis) and antibacterial activity. Stem extracts exhibit anti-enterovirus activity against anti-Coxsackie virus B3, Coxsackie virus B5, Poliovirus I, Echovirus 9, and Echovirus 29. Also possess antirheumatic, carminative, diuretic, and tonic properties. Treatment for sores, amenorrhea, metrorrhagia (irregular uterine bleeding), traumatic injuries, rheumatoid arthritis, and anemia
Syzygium buxifolium (leaf) [year-round] evergreen shrub	Taken as a febrifuge (reduce fever). Cooling effect when rubbed on the bodies of smallpox patients
Vaccinium bracteatum (leaf) [year-round] evergreen shrub	Radical scavenging activity and protection against KBrO3-mediated kidney damage. Anticancer and anti-inflammatory activity. Contains isoorientin, orientin, vitexin, isovitexin, isoquercitrin, quercetin-3-O-α-L-rhamnoside, and chrysoeriol-7-O-β-D-glucopyranoside

12.4 Future Research

This study was designed to evaluate the potential for self-medication in Tibetan macaques. At present we cannot completely rule out the possibility that macaques consumed some or all of these plants described above only to meet some micronutrient deficiency, or that the amounts consumed were insufficient to bring about physiological change. However, the evidence presented in this chapter is compelling enough to warrant further research.

Where do we go from here? In order to demonstrate therapeutic self-medication, there are four basic requirements: (1) identify the disease or symptom(s) being treated, (2) distinguish the use of a therapeutic agent from that of everyday food items, (3) demonstrate a positive change in health condition following self-medicative behavior, and (4) provide evidence for plant activity and or direct pharmacological analysis of compounds extracted from these therapeutic agents (Huffman 2010). The pharmacological activity reported here for 12 species is the first stage of fulfilling requirement (4). This suggests that ingesting these plants may elicit significant physiological benefit if ingested in sufficient amounts.

The broad spectrum of confirmed pharmacological activity reported here suggests several avenues of research to pursue in the future and reason to believe that Tibetan macaques self-medicate. Depending on the pharmacological activities of the plant in question, future work needs to attempt to directly link the context of use with the health status of the individual. This requires longitudinal investigation with attention to (1) seasonal influences (e.g., birth, mating, infection seasonality), (2) presence or absence of large-scale disruptive social influences likely to induce psycho-physiological stress (e.g., troop fission or the death of a leader or principle care-giver), (3) reproductive state (e.g., pregnancy, estrus, reproductive history), and (4) age and health status. Monitoring of identified individuals representative of all age-sex classes, recording reinfection seasonality, infection intensity and behavioral indicators of poor health, weakened body condition, poor appetite, plant food selection patterns, etc. are required. These data will help to provide the necessary context of medicinal plant use to strengthen the case for self-medication in Tibetan macaques (e.g., see Huffman et al. 1996a, b; Huffman and Caton 2001; Alados and Huffman 2000; MacIntosh et al. 2011; Burgunder et al. 2017). Only recently has the effect of seasonal dietary change on micro- and mycobiota composition of Tibetan macaques been investigated (Sun et al. 2016, 2018).

In closing, it should be noted that there are still other medicinal properties in the medicinal diet that have not been discussed in detail. They need to be looked at more closely in the future. These include the possible roles of anti-inflammation, immunoprotection, antibiotic, antibacterial, and antiviral properties, in the passive protection or treatment of seasonal afflictions brought on by cold-damp or hot-humid weather conditions. Do troop members ingest these items more in some seasons than others? Noteworthy too about these understudied properties of the diet are the widespread anticancer (antitumoral), osteoprotective, cardiovascular protective, and neuroprotective effects. Do older members of the troop ingest items with these properties more often than younger ones?

In the aging Western society today, such diseases form the core of many of our health problems, and it has been argued that the cause of this is due to the change in our diets, shifting towards more processed foods and away from more natural food sources (Johns 1990). The properties of the Tibetan macaque diet may provide us with important insights into the long-term dietary strategy of primates occurring at the interface of food and medicine.

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Appendix: Plant Secondary Metabolites in Plant Items Ingested by Tibetan Macaques at Mt. Huangshan

Abietane (diterpenoid)
Alkaloids
Essential oils
Flavonoids
Icariin (prenylated flavonol glycoside)
Icariside II (Baohuoside I) and Baohuoside II, III, V, VI
Isoflavones
i6-ethoxyca lpogonium isoflavone A, durmillone, ichthynone, jamaicin, toxicaro l
Isoflavone, barbigerone, genistein
Organic acids
Polysaccharides
Polyphenols
Saponic glycosides (hederagenin)
Stigmasterols
Terpenes

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