Christmas curiosity or medical marvel?

A seasonal review of mistletoe

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A fascinating feature of Christmas, mistletoe is a rather mysterious parasite with a complicated folklore and, perhaps, significant potential in medicine. This review concentrates on ***Viscum album***, the 'original' mistletoe. Its distribution and conservation in Britain, traditions and potential in medicine are considered within the wider context of the species worldwide.

Viscum album, (Figure 1) is just one of some 1300 mistletoe species worldwide. All are plant parasites, and in their native lands many have similar folklore and superstitions to our own British species. Mistletoes are the dominant members of the Santalales, a plant order containing mostly parasitic members. Others in the order include the Santalaceae (sandalwoods) and the Balanophoraceae. Mistletoes were once lumped into the Loranthaceae, but are now split into several separate families. The largest and most important of these are the Loranthaceae *sensu stricto* (over 900 species) and the Viscacaeae (over 400 species). Smaller families include the Eremolepidaceae and Misodendraceae.

Mistletoes are all hemi-parasites of trees and shrubs, joining to the host via an intimate xylem connection called a haustorium (see Box 1). Most take only water and solutes from the host, manufacturing their own metabolites through photosynthesis. Some, notably the forestry pest *Arcuethobium* species of North America, have reduced scale-like leaves and approach holoparasitism. The majority are aerial parasites, though a few, including the appropriately named Australian Christmas Tree *Nuytsia floribunda*, are root parasites. Most also have distinctive methods of seed dispersal, usually with distinctively sticky fruits that adhere to new host branches following dispersal by birds. *Arceuthobium* species disperse their seeds by squirting them from the fruits. A few genera (*Nuytsia* and *Misodendron*) have developed wind-dispersed seeds. Unusual pollination through animal interaction is characteristic of some species.

Despite their similarities, it seems that the Loranthaceae and Viscacae arose separately within the Santalales and their adaptation as aerial parasites is convergent. They have very different floral appearance, with the rather dowdy Viscaceae flowers (Figure 1) eclipsed by the elongate colourful flowers of the Loranths (Figure 2). The two families have similar worldwide distributions, occurring throughout the tropics and subtropics, including sub-Saharan Africa, Central and South America and Australasia. The Viscaceae also venture north into Europe and North America with 100 *Viscum* species in the Old World and 200 *Phoradendron* species in the New World.

Viscum has 45 species in Africa and 30 in Madagascar, with just a few of the *V. album* group spreading into temperate European and Asian areas. Though fairly uniform in its floral characteristics, the plant form varies from the familiar *V. album* through to *V. minimum*, an African species with much reduced leaves and stems, parasitic on fleshy *Euphorbia* species (Figure 3). *V. album* is the only mistletoe found in Britain, though others are found in continental

Title image: Viscum album, *Tenbury Wells mistletoe market.*

Figure 1. Viscum album *is a member of the Viscacaeae.*

Europe, including the red-berried *V. cruciatum* (Figure 4) in southern Spain. *Arceuthobium oxycedri*, one of the Dwarf Mistletoes more usually associated with North America, is found in the junipers of Greece, the Black Sea and a few Mediterranean sites. Also, a Loranthaceae member, *Loranthus europaeus*, grows on Fagaceae species, including oak, in southern and central Eastern Europe. European mistletoe taxa are further increased by subdivision of *V. album* into three subspecies:

- *V. a. platyspermum* (syn *V. a. album*) on deciduous hosts throughout Europe
- *V. a. abietis* on Firs in central and southern Europe
- *V. a. laxum* (syn *V. a. austriacum*) on Pine and Spruce in central Europe.

The Asiatic *V. album* populations belong to a fourth subspecies, *V a. coloratum*.

Mistletoe in Britain – hosts and distribution

Only *V. a. platyspermum* occurs in Britain. It is also widespread in continental Europe, though rare in the north and extreme south-west. The British distribution is centred in the south and west midlands, with particularly good populations in Herefordshire. This was first described by Bull, in 1864, who listed 30 host species in Herefordshire with a further 23 in other counties, but he emphasised that cultivated apple (*Malus domestica;* Figure 5) was by far the most popular (Bull, 1864). Today the host list stands at over 200 tree species.

The first national mistletoe survey in the early 1970s (Perring, 1973) mapped the species on a two by two km square (tetrad) basis and assessed host frequency. The results suggested that mistletoe distribution is influenced indirectly by man, as most records were of plants on non-native or planted trees. Cultivated apple was confirmed as the most frequent host, followed by hybrid limes (*Tilia spp),* hawthorn (*Crateagus spp),* hybrid poplars (*Populus spp)* and false acacia (*Robinia pseudacacia;* Figure 6). Mistletoe seems to prefer its hosts in an open situation rather than woodland, and so orchards, parkland and gardens are ideal, if somewhat artificial, habitats. Its distribution (Figure 7) was concentrated in Herefordshire, Gloucestershire, Worcestershire and Somerset, with scattered records elsewhere in the south, and rare occurrences in the north and east England, Wales, Scotland and Ireland. There are no straightforward explanations for this pattern. The core area contains apple orchards, but this cannot be the sole explanation because apple orchards are also frequent in the south-east. Rather, climate combined with host availability, are likely influences and are under investigation.

Figure 2. Tapinanthus sansibarensis, *an African member of the Loranthaceae, showing colourful flowers, characteristic of the family. Photo by Neil Bromhall.*

The most recent (1990s) national mistletoe survey aimed to build upon the 1970s analysis and assess whether British mistletoe was declining with the decline in traditional apple orchards. The survey, a public participation project, was organised by the Botanical Society of the British Isles (BSBI) and Plantlife. More than 12 000 winter sightings were sent in between 1994 and 1998. Results broadly confirmed the distribution patterns and host preferences of the 1970s study, but did not confirm a decline. Although many recorders' anecdotes suggested a local decline with orchard removal, the mistletoe distribution increased, particularly across the Midlands and southern England (Figure 7), possibly reflecting increased recording effort in the 1990s (Briggs, 1995 and 1999).

Figure 3. The African Viscum minimum *on* Euphorbia.

Although non-quantitative, the 1990s survey highlights differences across the country in habitat and host preference. Gardens topped the list of favourites (39%), followed by orchards (30%), then parks (12%) and woodland (5%). This emphasises the preference for open and man-made habitats. Within habitats, host preferences varied. Gardens had the longest host list with apple trees accounting for 65% of records. Orchard records were also dominated by apple (90%), park and churchyard records were mostly on hybrid lime (63%) and hedgerow records, largely hawthorn (50%).

Figure 4. The Spanish Viscum cruciatum *showing its red berries.*

These figures varied regionally: garden records were >60% in the east, south-east, north and extreme west; orchard records were highest in Herefordshire, and parkland records increased to 25% in the east. Host preference hierarchy altered accordingly, with proportion of lime rising to 25% in the east, reflecting the parkland records, and apple at >70% in the north. The longest host lists are in the stronghold areas, with mistletoe survival elsewhere closely linked to favoured hosts.

Animal associations

Nearly all mistletoe species rely on animals for pollination and seed dispersal, and most also provide food for animals, including several obligate mistletoe feeders. The seed dispersers are almost exclusively birds. The few exceptions include *Dromiciops australis*, an Argentinean tree-climbing marsupial that spreads the seed of *Tristerix corymbosus*. Whichever vector species, dispersal and 'planting' are always achieved by glueing the sticky berries to potential host trees, either through wiping the sticky seed from beaks or by defecating partially digested fruit.

Figure 5. Viscum album *growing on its favourite host, cultivated apple.*

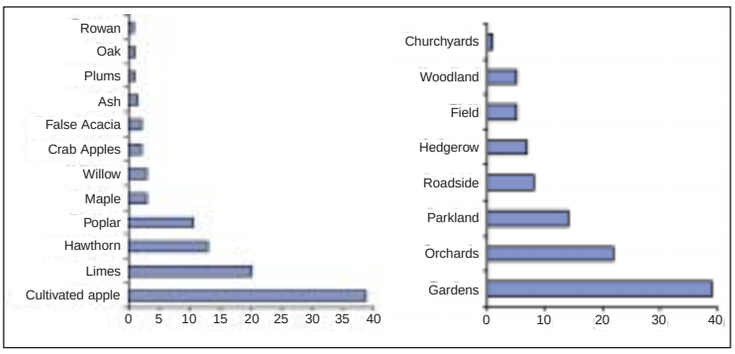

Figure 6. Viscum album *host (left) and habitat (right) preference across Britain. Data from the 1990s survey.*

In Europe the main vectors are the mistle thrush (*Turdus viscivorous*), a defecating vector, and blackcap (*Sylvia atricapilla),* a beak-wiping vector. Usually, only mistle thrush overwinters in Britain and is our main vector. Some studies suggest that other birds fail to recognise the white (as opposed to orange, red or black) berries as food. Curiously, the etymology of *Turdus viscivorous* suggests it was named after its fondness for the red *V. cruciatum* berries rather than the white *V. album*.

Mistle thrush's common occurrence outside the ranges of both European *Viscum* species suggests that it is not a dedicated mistletoe specialist. It is certainly an inefficient vector, tending to defecate long strings of seeds held on threads of viscin, with only one or two attaching to the host branch. In contrast, the Australian mistletoe bird (*Dicaeum hirundinaceum*) carefully 'wipes its bottom' on a branch each time it passes a seed. In continental Europe, Blackcaps are also much more efficient, wiping each seed onto a branch from their beaks. Recent changes in Blackcap wintering patterns have led to some wintering in Britain, particularly in the mistletoe-rich Severn Vale. The long-term implications of this for mistletoe distribution are unknown, but intriguing.

For pollination, many species, including *V. album*, rely on insects. This may seem an odd strategy for *V. album*, a winter-flowering dioecious species with tiny green unattractive flowers. Wind pollination seems more likely but examination of the flowers in February usually reveals small flies such as *Dasyphora* species, attracted by scent and nectar. Pollination mechanisms for some African and New Zealand loranths are quite sophisticated, relying on particular bird species to open the flowers and trigger the release of a cloud of pollen. These species rival the Orchidaceae in their specialist animal-dependency (see Kirkup in Polhill, 1998).

Mistletoes, generally, attract herbivores. Berries are an obvious food source but foliage is also attractive and more succulent than host foliage. Some species have developed host mimicry to reduce grazing by herbivores; others (*e.g.*, Mesquite mistletoe, a Texan *Phoradendron* species) may be used as a forage crop by farmers.

Some invertebrate herbivores, including several hundred lepidopterans, are obligate mistletoe specialists. Examples include: many Australian Jezebels (*Delias* spp*)*; mistletoe browntail moth (*Euproctis edwardsii*); several North American hairstreak butterflies including the great purple (*Atlides halesus*), Thicket (*Callophrys spinetorum*) and Johnson's (*Mitoura johnsoni*), and the British tortrix moth (*Celypha woodiana*) (Figure 8*)* whose larvae are leaf miners in *V. album* leaves.

There are, presumably, many more mistletoe invertebrates that get less attention than butterflies and moths, or are difficult to sample from mistletoe high up in trees, leading to under-recording of, even very common, species. This is neatly demonstrated in Britain, where we have 'at least' three mistletoe bugs and one mistletoe weevil. All are probably under-recorded. Of the bugs, one is the plant-sucking homopteran, *Psylla viscid*. The others are heteropterans, *Anthocoris visci* and *Orthops viscicola*. Both seem to be associated with the psyllid, with *Anthocoris* probably feeding on it. *Orthops* was recorded as a new species in France in 1888, and within six months enthusiastic Herefordshire naturalists had undertaken surveys and recorded it as common – though they had obviously overlooked it before. Over a century later, the mistletoe weevil *Ixapion variegatum* was recorded in an orchard in Herefordshire, as a new British species, by National Trust surveyors. This species was also previously known in France – we must wait to see if it too becomes regarded as 'common'!

Viscum album outside its main range

There are many small *V. album* populations outside their main range, most arising from deliberate introductions. Two are in North America, far from their native area. Others are much more ' local' since most, if not all the populations in the east, north and extreme west of Britain, must be considered introductions. Populations in America include a flourishing colony in Sonoma County, California. Established by the eminent botanist Luther Burbank about 1900, this population has now spread through an area of over 200 km^2 and to many different hosts. In contrast, the other population, on Vancouver Island, British Columbia, has spread to only a few trees in the immediate vicinity despite being established for some decades (Job Kuijt, pers comm). Similarly, in Edinburgh, UK, mistletoe is confined to a few single plants in private gardens, with only small colonies in the Botanic Garden and the Dean cemetery. A local botanist, William Paxton (buried close to the colony in the Dean) introduced mistletoe to some of these sites in the 1890s – but they have not spread far in 100 years. In the Dublin Botanic Garden, a small 19th century colony has hardly spread despite a plethora of potential hosts nearby. By contrast, in the Botanic Garden in Cambridge, also outside the usual range, mistletoe grows on a large range of different host trees.

Figure 7. Tetrad map of Viscum album *distribution in Britain from the 1970s (left) confirmed in the 1990s (right) but with more records from the east and south east.*

Recent studies of mistletoe colonies in Hamburg and Brussels, both on the edge of *V.album*'s continental distribution, have confirmed that whilst spread may be very slow, the species is extremely persistent once established. The Brussels study (Olivier, 1998) details long-established populations in the city's cemeteries. Mistletoe records here show the plant is confined to certain areas and habitats. In Hamburg, several populations established in about 1903 (Poppendieck and Petersen, 1999), have spread only within a few hundred metres of their origin.

Similar studies are now underway in London, as part of the Greater London Biodiversity Action Plan (London Biodiversity Partnership, 2001). London has sporadic private garden mistletoe records but larger historic colonies, centred on Bushey and Home Parks (Richmond), and Myddelton House and Forty Hall (Enfield). The long-established Park populations are almost certainly introduced. The Enfield populations were established by, or at least encouraged by, E A Bowles (1864–1954), the plant breeder and garden writer, who lived at Myddelton House all his life.

Myths and traditional uses

Mistletoe appears in legends in many cultures. There are many common themes; our kissing custom is probably a remnant of an ancient fertility tradition, helped along by some British re-invention in the 18th and 19th centuries. In Greece, Aeneas was guided to the abode of the dead by plucking the 'Golden Bough' of mistletoe. The Norse God, Balder, was slain by an arrow of mistletoe, soon after everything living or growing in the earth had sworn not to harm him. In Britain, it is well known that the druidic priesthood valued mistletoe, both as a peace symbol and in medicine. They harvested it with a golden sickle, never letting it touch the ground and prized mistletoe on oak, their sacred tree, especially highly. Modern druids have resurrected their reverence of mistletoe oaks, and actively seek them out. Other religions are more suspicious, and the Church of England still actively discourages mistletoe in its churches.

Myths change as they pass down through generations. The druid story is often reported as factual, despite having only Roman accounts and much 're-discovery' of druidic customs in the 18th century by William Stukeley and others, but as an evergreen parasite growing high on deciduous hosts, it could appear to symbolise the life-force of the host through the winter months. The fertility imagery is heightened by *V.album's* shape: the paired leaves, berries and sticky white juice might just be said to resemble sexual organs.

The British midland custom of hanging mistletoe all year and ceremonially replacing it each Christmas, whilst burning the original, has now been lost. The kissing tradition, once largely confined to Britain, is now established in all English-speaking countries, even if they do have to make do with 'incorrect' local mistletoe species. Seasonal trade, to satisfy this habit, is now considerable, with Britain relying on imports from France, and much of America relying on material harvested in Texas. 'Inconvenient' customs, such as removing a berry after each kiss and thus limiting the fun, are usually forgotten.

Figure 8. Mistletoe tortrix moth, Celyhpa woodian. *From Bristol City museum collection. Photo by Raymond Barnett*

Mistletoe traditions in continental Europe can differ, with use at New Year rather than Christmas. New traditions can still arise. In the current plantlife campaign to nominate county flowers, there has been competition between Herefordshire, Worcestershire and Gloucestershire to have mistletoe as 'theirs'. In the US, mistletoe is already the 'state flower' for Oklahoma. But the principal 'new' use for *V. album* may turn out to be in medicine – Getafix's (the druid of the Asterix cartoon) magic potion may have potential after all.

Mistletoe in medicine

Sir John Colbatch, writing in 1720, suggested that '*there must be something extraordinary about that uncommon beautiful plant, that the Almighty had designed it for further and more noble uses than barely to feed thrushes or to be hung up superstitiously*'. His experiments were on epilepsy, and he was just one of many mistletoe researchers throughout the 18th and 19th centuries, particularly in German-speaking parts of Europe. It was there that Rudolf Steiner made his extraordinary predictions about the plant in the 1920s. He believed that, as a parasite, the plant should have medicinal value against cancer, and he described methods of producing extracts for such use. Since then, there has been considerable use of mistletoe in both conventional and anthroposophic medicine, with many mistletoe products and extracts now used in cancer therapy as well as for hypertension, arteriosclerosis and arthritis (reviewed by Bussing, 2000).

The components thought to be active in cancer therapy and some of the products available have been evaluated. *V album's* anticancer properties arise from a mix of cytotoxic and immuno-modulatory compounds, including the Viscotoxins and mistletoe lectins. The viscotoxins (I, II III *etc*) are thionins that seem to exert cytotoxicity by rapid permeabilisation of cell membranes. The mistletoe lectins, related in structure to ricin (from *Ricinus)* are Type 2 ribosome-inactivating proteins (RIPs). Each consists of two polypeptide chains (A and B). Several different types have been identified, known simply as ML I, II *etc*. These are also cytotoxic and are effective immuno-modulators, with uses in site-directed immunosuppression. They have been extensively researched – both in terms of biological action and structure (reviewed by Pfuller, in Bussing, 2000).

The Viscotoxin and ML complement of *V. album* vary with the season, host and subspecies, and so most proprietary mistletoe extracts use a blend from different sources and seasons. These extracts, manufactured by German and Swiss institutes (products include: Abnoba, Helixor, Iscucin and Iscador) are mostly used in anthroposophic and complementary cancer therapy in continental Europe. Clinical trials involving the extracts (and isolated Viscotoxins and ML) have not yet confirmed their value. Though many have reported improved quality of life and tumour regression, trial quality is often poor and the mixture of products used makes comparison difficult (see Bussing, 2000 and the *www.cancer.gov* website).

Mistletoe is also available as herbal remedies, usually in the form of a tea, primarily for hypertension. The teas are widely available in continental pharmacies but are relatively infrequent in Britain. Despite its medical potential, the most common consumer use of *V. album* in Britain may well be in shampoo, as it is an ingredient in several supermarket products.

Box 1. From berry to plant

Viscum album seeds tend to germinate in February and March after the berries have become attached to host branches. Each berry is single-seeded but they are often polyembryonic and can produce more than one hypocotyl (Figure 9). These green hypocotyls, which bend towards the host bark surface, are the only non-parasitic phase of the plant. They flatten to a sucker-shaped holdfast against the bark and then gradually penetrate to the host cambium. There are many studies of the mechanism of penetration – some are reviewed in Bussing (2000).

Figure 9. Germinating seed showing two hypocotyls developing holdfasts.

Vascular links can take several months to establish, and aerial growth is negligible in the first year. During this time, an invasive organ known as a haustorium develops under the bark. This fuses with and grows in synchrony with the host wood. Haustorial structure varies between plants but often distorts the host wood (becoming a large plant gall) at the point of infection, often at the expense of the distal portion of the infected branch.

Figure 10. Haustorial cross-sections: TS of the host (and LS of the mistletoe), showing distorted host wood and fused cambial tissue.

In *V. album* the primary haustorium develops by stimulating the host cambium and growing with it to form a wedge-shaped 'sinker' embedded in new host wood. This effectively grafts the mistletoe onto the host (Figure 10). The primary haustorium also extends laterally, producing cortical strands under the host bark. These produce secondary haustoria and new mistletoe shoots some distance away from the original point of infection. Several growths on one branch may be linked by these cortical strands, which can often be traced where they pass under the bark.

The aerial portion of *V. album* plants has characteristic forked branches, each tipped with a distinctive pair of leaves (Figure 1). Each branch divides once each year, so that whilst initial growth is slow – only one pair of leaves after year 1 and two pairs after year 2, subsequent growth becomes very rapid. The branching habit means that intact, unpruned *V. album* can form apparently spherical growths. Flowers develop on each branch in mid-winter, with male and female on different plants. Both sexes are small and green and often overlooked, even though present as buds (Figure 1) in Christmas mistletoe. The terminal flowers open whilst last year's berries, by now positioned in branch axils, are still on the plant. The next season's berries develop through the summer months as green berries, only ripening to white in winter.

Conservation, control and harvesting

Publicity arising from the 1990s survey led to a widespread belief that mistletoe in Britain is under threat. As we have seen, results suggest this belief is erroneous, at least in distribution terms. The issue of reduced population density through orchard decline is gradually being addressed by the inclusion of mistletoe (and mistletoe invertebrate) conservation in restoration initiatives for traditional orchards.

There are also conservation initiatives for some unusual mistletoe colonies, including replacement of a lost colony in the Botanic Garden and introduction at a local arboretum in Hamburg, with transplanted trees infected with mistletoe (Poppendieck and Petersen, 1999). In London, conservation of existing colonies and establishment of new ones is an objective of the local Biodiversity Plan. Trial plantings, begun in 2002/3, are in sites chosen for ease of monitoring and management, including Enfield Lock, Haringey Railway Fields Nature Reserve and Chelsea Physic Garden.

Biodiversity conservation is not the only reason for new colony establishment. In France, researchers from Institut Hiscia (Switzerland) have a programme to increase *V. album* on selected oaks and elms. This is to ensure supplies of oak and elm mistletoe to contribute to cancer therapy extracts. Globally, however, mistletoe conservation is an infrequent issue. Mistletoe *control* is a much greater issue with many species seen as pests, reducing timber yields in commercial forestry, or fruit yields in orchards and causing distortion of specimen trees. Mistletoe will reduce both yield and tree size, though it is only major infestations that threaten the survival of the tree itself. Chemical control is not easy, as herbicides can also damage hosts, and physical control by pruning is often impractical or ineffective, as subcortical strands below host bark will regrow. However,

Box 2. Growing your own

To succeed in growing your own mistletoe you'll need to:

- Be prepared – success rates are low and so you'll need a lot of berries
- Time it right – success is much higher in February and March
- Be patient – mistletoe grows slowly in the first 4 years

First, secure a berry source. Berries collected at Christmas can be stored in a shed until mid-February but it is far better to use fresh berries. Next, choose your host, bearing in mind *V. album*'s preferences: apple first, then poplars, limes, false acacia, hawthorn etc. Most shrubs of the Rosaceae are suitable. Don't choose your favourite prize-winning fruit tree, as the mistletoe will distort growth and reduce yield.

Then prepare the berries. Stored berries will need rehydrating for a few hours in water. Whether fresh or stored, the seed needs to be squeezed out of the berry, along with a quantity of the sticky viscin. Try to plant at least 20 berries at once, as most will die or be eaten. Since *V. album* is diocieous, you'll need at least two plants for future berries. I advocate 'nature's way', emulating the mistle thrush and blackcap, by smearing berries onto the branch. Cutting a slit, as occasionally recommended, can also open the host to other infections. Stick each seed, with its own glue, to branches 1.5 metres or so up the tree and on the side or underside of a branch of at least 20mm diameter. Mark each berry loosely with string to aid monitoring.

Germination is fairly rapid and a short green hypocotyl should appear and bend to contact the host bark. At this stage, the tiny plants are particularly susceptible to grazing invertebrates and birds, and prone to dehydration until they have made a host connection. If all goes well, the hypocotyl should become erect and remain unchanged until the following Spring, when the first leaves appear.

for *V. album* at least, traditional control by selling 'prunings' at Christmas can be an ideal way to reduce parasite impact, provide additional seasonal income and ensure continued co-existence of both tree and parasite. Mistletoe prunings from Hereford and Worcestershire orchards are traditionally sold at the annual mistletoe auctions at Tenbury Wells. Although local harvestings occur throughout Britain, much of our Christmas mistletoe is imported from France, where *V. album* is more plentiful.

Conclusions

The more we find out, the less we seem to know about *V. album*. Surveys and analyses confirm previous distributions, but cannot explain the pattern. Mistletoe-dependent insects are under-recorded, with no real knowledge of their importance or biology. Conservation initiatives are based more on the species' cultural, than biodiversity, value. The varying European traditions are intriguing, with more serious mistletoe use in medicine in German speaking areas and, consequently, more publicity and published research in German. The recent English-language review (Bussing, 2000) gives a good review of current continental research – and demonstrates that there is a lot more to mistletoe than just Christmas kissing. Our mistletoe traditions may be contrived – but they're fun, and mostly harmless.

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www.rms.nau.edu/mistletoe/
The 'Mistletoe Center', maintained by Brian Geils, RMRS Flagstaff Lab. Excellent resource site, with publications *etc*.

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