GINKGO BILOBA

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1. THE EVOLUTION, ECOLOGY, AND CULTIVATION OF *GINKGO BILOBA*

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EVOLUTIONARY HISTORY

Ginkgo biloba, which is not closely related to any other living plant, is generally classified in its own division, the Ginkgophyta. This taxon is distinguished from the Coniferophyta (conifers) on the basis of its reproductive structures, most notably its multiflagellated sperm cells, and from the Cycadophyta (cycads) on the basis of its vegetative anatomy (Wang and Chen, 1983; Gifford and Foster, 1987). Recent molecular analysis of the Ginkgo genome, while far from complete, suggests a much closer relationship to the cycads than to the conifers (Hasebe, 1997).

The fossil record of the genus Ginkgo is extensive, with numerous reports of "Ginkgophyte" foliage and wood from many stratigraphic regions in both the northern and southern hemispheres. Because most of this material is sterile, however, its precise relationship to the extant species has always been conjectural. This uncertainty has recently been resolved by the discovery in Henan Province, China of fossils from the Middle Jurassic (180 million years ago) that possessed Ginkgo-like ovule-bearing organs (Zhou and Zhang, 1989). These are the earliest, unequivocal representatives of the genus Ginkgo and have been described as a new species, *G. yimaensis*, that differs from *G. biloba* in having more highly dissected leaves and much smaller ovules clustered on branched peduncles (Figure 1). Another extinct "species," *G. adiantoides*, had an extensive distribution in the northern hemisphere from the lower Cretaceous through the Pliocene (141–1.8 mya), and many authors consider this taxon to be the likely ancestor of *G. biloba* because it had a similar leaf morphology and ovule structure (Tralau, 1968; Zhou, 1994).

The genus Ginkgo appears to have reached the peak of its diversity during the lower Cretaceous (141–98 mya), with several distinct species occupying a more or less circumpolar distribution in the northern hemisphere which also extended into several parts of the southern hemisphere. During the upper Cretaceous (98–65 mya), the fossil record for Ginkgo shows a decline in diversity and distribution, particularly toward the end of the period when worldwide temperatures decreased dramatically.

The diminution of Ginkgo's range continued into the Tertiary, and was particularly striking from the Oligocene (38–26 mya), when the genus disappeared from

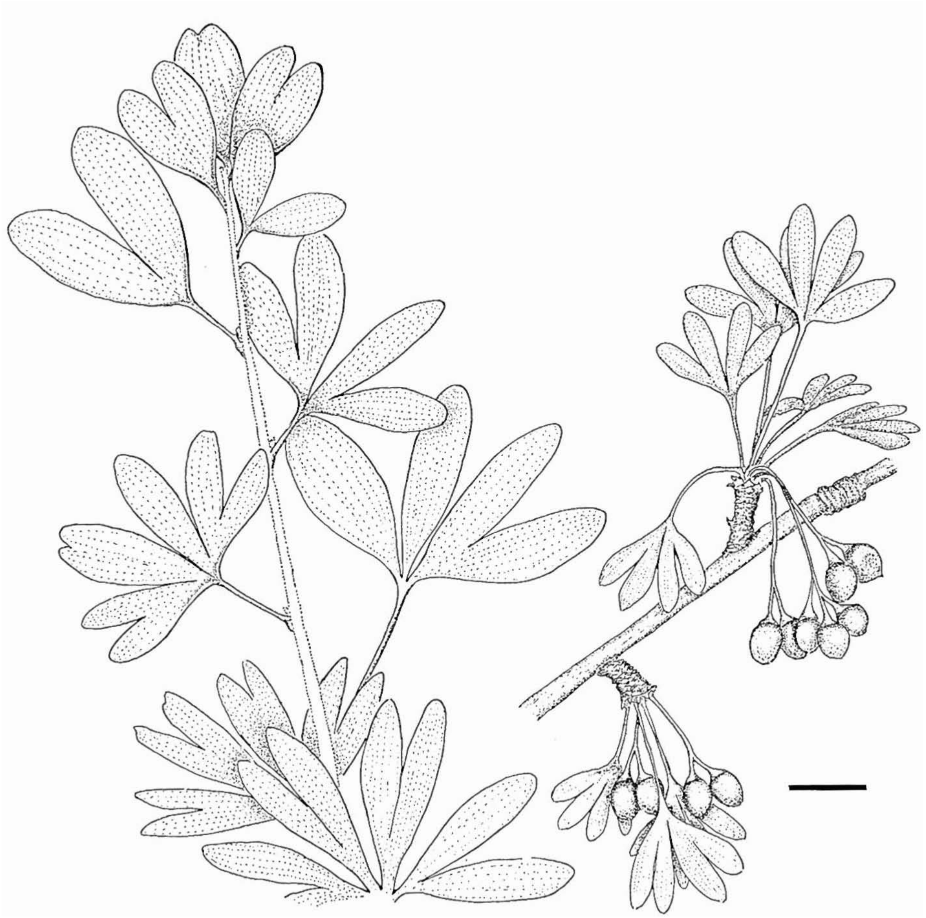

Figure 1 A reconstruction of *Ginkgo yimaensis*: left, leaves of various shapes and sizes believed to have been produced by a single long shoot; right, a portion of a long shoot with two dwarf shoots bearing both leaves and ovule-bearing organs. Bar at lower right equals three centimeters. Reprinted with permission from Zhou and Zhang, 1989.

polar areas, through the end of the Miocene (24–7 mya), when it disappeared from western North America. These dramatic changes were most likely the result of the extensive cooling that occurred throughout the Northern hemisphere during these time periods. The genus Ginkgo was gone from Europe by the end of the Pliocene (1.8 mya) as temperatures dropped and the rainfall regimen gradually shifted from one of summer-wet to one of summer-dry. The only known Pleistocene (1.8 mya to present) occurrences of the genus Ginkgo are from southwestern Japan. Based on their leaf characteristics, these fossils have been classified under the name of the extant species, *G. biloba* (Uemura, 1997). In general, the distribution of Ginkgo fossils indicates that the genus has been relatively consistent in its ecological tolerances since the Cretaceous, preferring to grow in warm temperate climates characterized by moist summers and cool winters (Tralau, 1968; Uemura, 1997). As regards the morphology of its reproductive organs, the trend within the genus Ginkgo seems to be one of reduction, with the ovules decreasing in number while increasing in size, and the pedicels disappearing to leave sessile ovules connected directly to the peduncle (Zhou and Zhang, 1989; Zhou, 1991; 1994).

ECOLOGY

As a wild species, *Ginkgo biloba* is native to China and was probably a member of the mixed-mesophytic forest community that once covered the hill country bordering the Yangtze River valley. Most of this warm-temperate forest has now been cut down with the exception of a few remnants located in isolated valleys and on steep mountain slopes (Wang, 1961; Zheng, 1992a). One of Ginkgo's last wild refugia is thought to be in Zhejiang Province, China, on the west peak of Tianmu Mountain (Xitianmu Shan: 1506 meters elevation; 119° 25′ E; 30° 20′ N; mean annual rainfall 1767 millimeters; mean January temperature –3.2° C; mean July temperature 20.5° C). There are also reports of "wild" Ginkgo populations in other parts of China, including Guangxi, Guizhou and Sichuan Provinces, but these claims have yet to be substantiated by careful field research (Liang, 1993).

Botanists have long debated the "wildness" of the Ginkgo population growing on Tianmu Mountain. While the long history of human habitation in the area makes it difficult to determine whether or not the trees are truly wild, the exceptional species-richness of the surrounding forest and the large size of many of its trees suggests that they may well be (Del Tredici *et al.*, 1992; Zheng, 1992b). Recent isozyme studies on the population, indicate a relatively low degree of genetic diversity among the plants, an observation that led the authors to speculate that the population may be descended from cultivated trees (Wu *et al.*, 1992).

In 1984, the Tianmu Ginkgo population consisted of approximately 244 individuals with a mean diameter at breast height (DBH) of 45 centimeters and a mean height of 18.4 meters. Most of the trees were growing on disturbed sites such as along stream beds, on rocky slopes, and on the edges of exposed cliffs (Figure 2). Ginkgo seedlings were quite rare on Tianmu Mountain and are typically found in areas of the forest that have been opened up by disturbance, an observation that provides support for the idea that Ginkgo acts as a "pioneer" species in its native habitat (Del Tredici *et al.*, 1992).

Approximately 40% of the Tianmu Ginkgos possessed more than one trunk greater than 10 centimeters diameter at breast height (DBH). Most of these secondary trunks originated from lignotubers located at, or just below, ground level (Figure 3). Secondary trunk formation was most apparent in specimens that were damaged or under severe stress (Del Tredici *et al.*, 1992). The sprouting ability of Ginkgo is an important factor that has enabled the species to persist on the mountain's badly eroded slopes, and may well have played a role in the survival and morphological stability of the genus since the Tertiary (Figure 4).

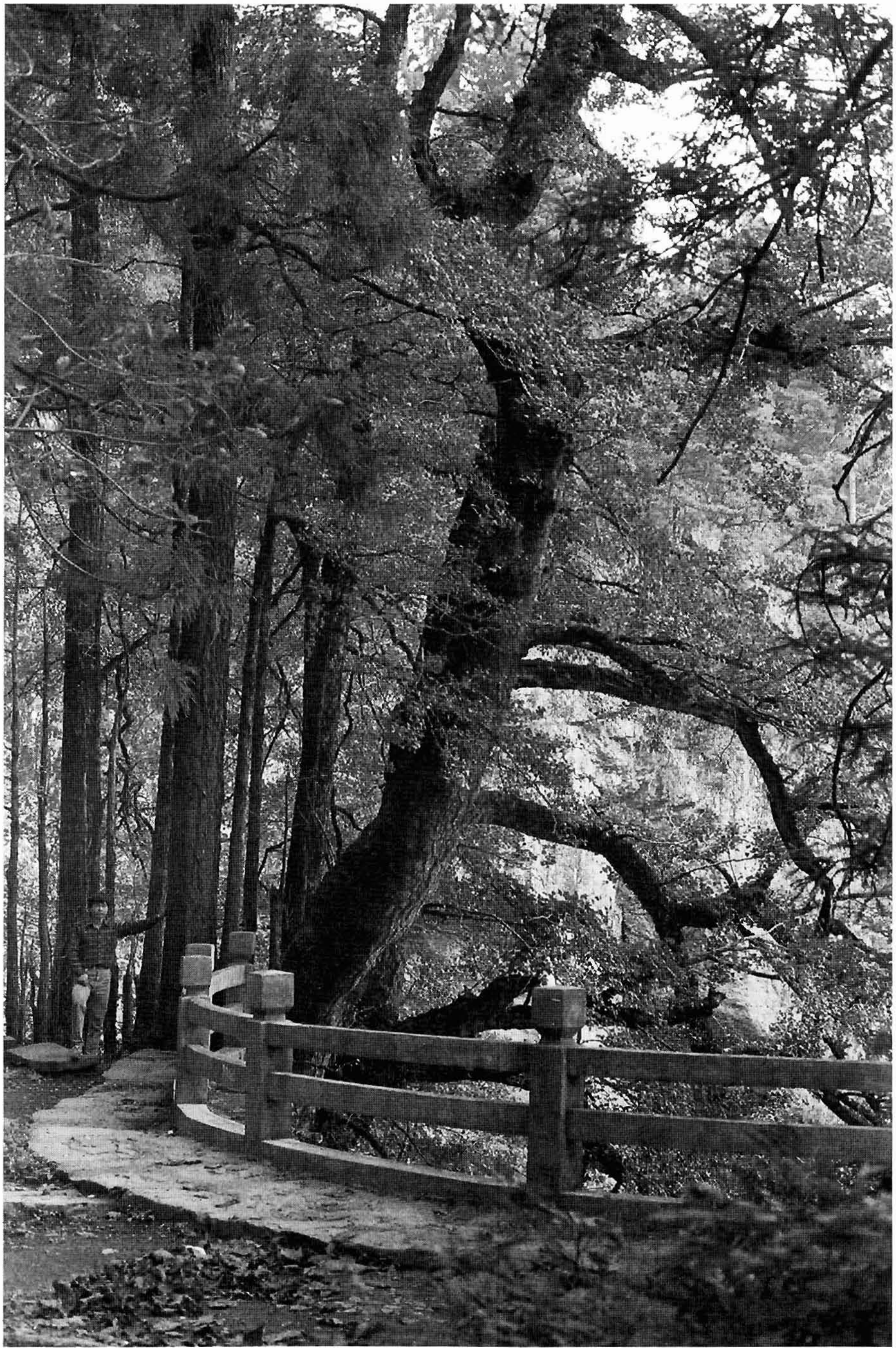

Figure 2 The famous "living fossil" Ginkgo tree growing on Tianmu Mountain, Zhejiang Province, China, photographed in 1989. This ancient, ovulate specimen occupies an area of approximately 20 square meters and consists of 15 stems greater than 10 centimeters diameter. The largest trunk has a diameter of 110 centimeters. The Chinese describe this tree, perched on the edge of a steep cliff at 950 meters elevation, an "an old dragon trying to fly." The fence protecting the tree was built in 1980. Reprinted from Del Tredici *et al.*, 1992.

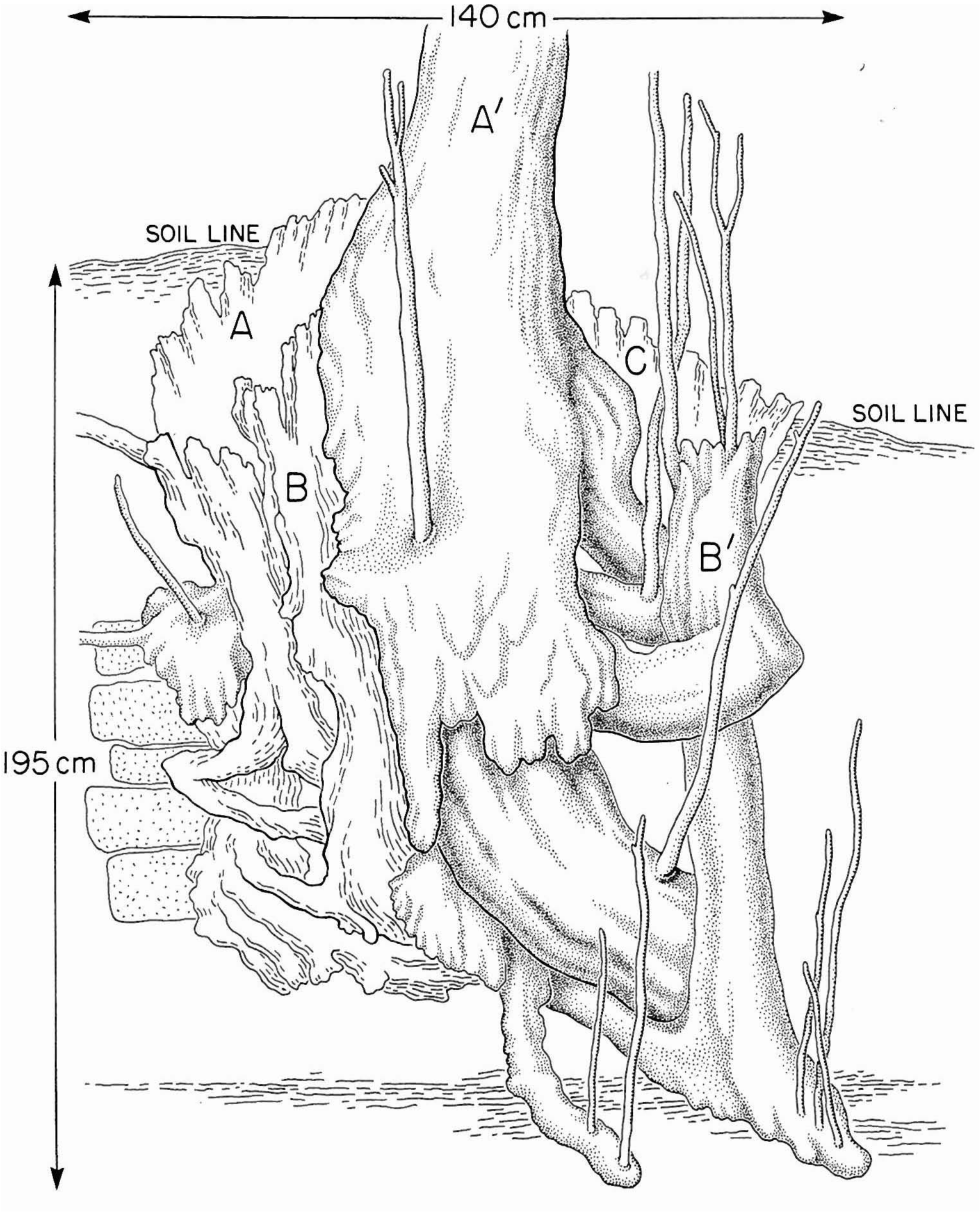

Figure 3 The lignotuber-developed shoot system of an old Ginkgo growing on top of a stone wall on Tianmu Mountain in Zhejiang Province, China. At least three generations of stems can be seen: the oldest represented by the cut trunks A, B, and C (with diameters of 55, 40 and 37 centimeters respectively); the second by the living trunks A′ and B′ (with diameters of 26 and 20 cm); and the third by suckers arising from the distal portions of the lignotuber (stippled). Reprinted from Del Tredici *et al.*, 1992.

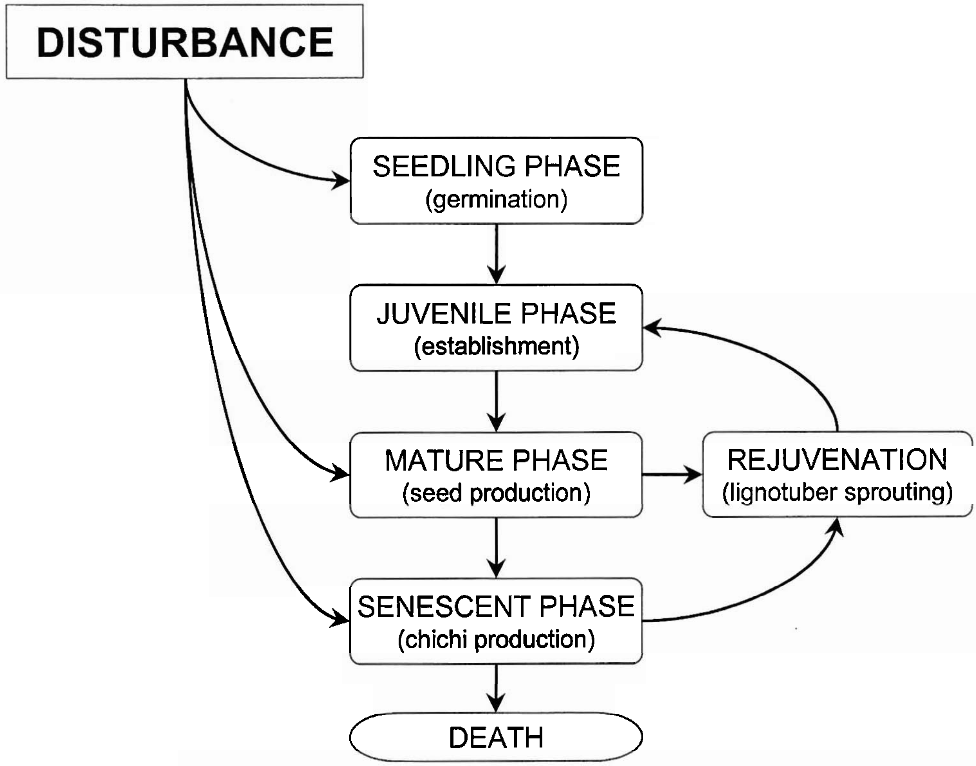

Figure 4 A schematic representation of the life cycle *of Ginkgo biloba* on Tianmu Mountain.

Sexual Reproduction

Ginkgo is a dioecious species, with separate male and female individuals occurring at a roughly 1:1 ratio, although occasional monoecious individuals are reported to occur (Santamour *et al.*, 1983b). Ginkgo shows a long juvenile period, typically not reaching sexual maturity until 20 to 30 years of age. Male and female sex organs are produced on short shoots, in the axils of bud scales and leaves. The male catkins emerge before the leaves and fall off immediately after shedding their pollen. Wind pollination occurs anywhere from early April in areas with mild winters to late May in areas with severe winters. As to pollination distance, it is difficult to say what the maximum is, but in the Boston area 400 meters between male and female trees does not inhibit seed set (Del Tredici, 1989).

Ginkgo ovules are 2 to 3 mm long and produced in pairs at the ends of stalks 1 to 1.5 centimeters long. When the ovule is receptive, it secretes a small droplet of mucilaginous fluid from its micropyle which functions to capture airborne pollen. Retraction of this droplet at the end of the day brings the pollen into the pollen chamber. Once inside the ovule, the male gametophyte commences a four-month long development period that culminates with the production of a pair of multiflagellated spermatozoids, one of which fertilizes a waiting egg cell (Friedman, 1987) while the ovules are still on the tree (Holt and Rothwell, 1997). Depending on the date of pollination, this union can occur anytime between late August to late September.

The mature seed of Ginkgo is relatively large (20–30 mm × 16–24 mm) and consists of an embryo embedded in the tissue of the female gametophyte surrounded by a thick seed coat. This seed coat consists of a soft, fleshy outer layer (the sarcotesta), a hard, stony middle layer, and a thin, membranous inner layer. The seed, devoid of the fleshy sarcotesta, is generally referred to as the Ginkgo "nut," with dimensions of 19–30 mm × 11–14 mm. The developing ovules are green until they mature in the autumn when, in response to cold temperatures, they turn the same yellow color that the leaves do. Typically they fall from the tree about a month after fertilization. The foul odor associated with Ginkgo seeds develops only when they are fully mature, and is the result of the presence of two volatile compounds, butanoic and hexanoic acids, localized in the sarcotesta (Parliment, 1995), also contains phenolic compounds known to cause contact dermatitis in humans (Kochibe, 1997).

Seed Dispersal and Establishment

The paucity of fossilized Ginkgo seeds has not deterred speculation as to what animals might have dispersed Ginkgo seeds over the course of its long evolution. Several authors have proposed that dinosaurs might have dispersed Ginkgo seeds, but none of them have provided any anatomical evidence that would support the claim or specified what type of dinosaur it might have been (Janzen and Martin, 1982; van der Pijl, 1982; Tiffney, 1984; Rothwell and Holt, 1997). A second proposal is that early mammals in the extinct family Mutituberculata could have been effective dispersal agents (Del Tredici, 1989). These marsupial-like creatures, often referred to as the "rodents of the Mesozoic," were widespread in the temperate parts of the northern hemisphere from the Late Jurassic through the Oligocene. Many multituberculates possessed teeth that were adapted to cracking hard food objects, such as seeds, and a skeletal structure that was adapted to living in trees (Krause and Jenkins, 1983).

In modern times, a number of different mammals have been observed feeding on, and presumably dispersing, the odoriferous, nutrient-rich seeds of *G. biloba*. In the order Rodentia, these include the red-bellied squirrel (*Callosciurus flavimanus* var. *ningpoensis*, family Sciuridae) on Tianmu Mountain (Del Tredici *et al.*, 1992), and the gray squirrel (*Sciurus carolinensis*, family Sciuridae) in eastern North America (Del Tredici, 1989). In the order Carnivora, potential dispersal agents include the masked palm civet (*Paguma larvata*, family Viveridae) on Tianmu Mountain (Del Tredici *et al.*, 1992), the leopard cat (*Felis bengalensis*, family Felidae) in Hubei Province, China (Jiang *et al.*, 1990), and the raccoon dog (*Nyctereutes procyonoides*, family Canidae) in Japan (Hori, 1996). The existence of three independent reports of carnivores consuming whole Ginkgo seeds and defecating intact nuts, raises the possibility that the foul smelling sarcotesta may be attracting these animals by mimicking the smell of rotting flesh (Del Tredici *et al.*, 1992). Projecting this line of speculation back into evolutionary time, it seems likely that if dinosaurs were involved in the dispersal of Ginkgo seeds, then it was probably done by carrion feeding scavengers, with teeth adapted to tearing flesh, rather than by herbivores with dentition adapted to grinding vegetation (Del Tredici, 1989).

Ginkgo seeds are dormant when they fall from the tree because the embryo is not fully developed, being only about 4 to 5 millimeters in length. If seeds are collected shortly after dispersal, cleaned, and placed in a warm greenhouse, the embryo will grow to its full size – 10 to 12 millimeters in length – and germinate within eight to ten weeks (Li and Chen, 1934; Holt and Rothwell, 1997). This type of germination behaviour has important implications in terms of seedling establishment in the field. In warm-temperate climates Ginkgo seeds are shed in late summer or early fall, and the embryo is able to make considerable growth during the mild weather that follows. In cold-temperate climates, on the other hand, seeds are shed later in the season and the colder autumn temperatures delay full embryo development until the following spring. This differential timing of embryo maturation means that seeds in warm climates will be ready to germinate during the favourable conditions of mid- to late spring (April through early June), while those in cold climates will not germinate until later in the summer (late June through early August), when conditions for establishment are much less favorable (Del Tredici, 1991a). These phenological differences suggest that the innate germination requirements of Ginkgo seed may account for the species' warm-temperate distribution in recent times, as well as the warm-temperate distribution of its fossil ancestors.

Tree Architecture

Ginkgo is an extremely long-lived deciduous tree that, in cultivation in China, is capable or reaching ages in excess of a thousand years, with stem diameters between one and four meters (Lin, 1995). Depending on the growing conditions, mature trees typically reach heights of between 20 to 40 meters, although one exceptional specimen in Korea has been reported with a height of 64 meters and a girth of 14 meters (Del Tredici, 1991b). The form of vigorous young Ginkgos is distinctly pyramidal, with a dominant central leader and widely spaced whorls of lateral branches that grow out at a diagonal orientation to the trunk. With the onset of sexual maturity, at around 25 years of age, height growth generally slows down and the tree fills in its sparsely branched juvenile structure, forming a broad, spreading crown (Gunkle *et al.*, 1949; Del Tredici *et al.*, 1991c).

Ginkgo trees produce two types of shoots: long shoots with widely spaced leaves that subtend axillary buds; and short, or spur, shoots with clustered leaves that lack both internodes and axillary buds. Long shoots are responsible for building up the basic framework of the tree and generating new growing points, while the short shoots produce the majority of leaves and all of the reproductive structures. In response to a variety of environmental and physiological factors, the growth pattern of these shoots can be reversed, such that a short shoot can proliferate into a long shoot, and the terminal growth of a long shoot can fail to elongate and become a short shoot (Gunkle *et al.*, 1949). This flexibility provides Ginkgo with a simple mechanism for modulating carbohydrate allocation between sexual reproduction and vegetative growth (Del Tredici, 1991c).

Under stressful growing conditions, Ginkgo is capable of producing secondary trunks at or just below ground level. Typically, these secondary stems originate from root-like, positively geotropic shoots known as lignotubers or "basal chichi." Anatomically lignotubers develop in all Ginkgo seedlings as part of their normal ontogeny from buds located in the axils of the two cotyledons (Figure 5). When stimulated by some traumatic event, one of these cotyledonary buds often grows out from the trunk to form a woody, positively-geotropic lignotuber which has the capability of producing both aerial shoots and adventitious roots (Del Tredici, 1992; 1997). Similar structures, known as "aerial chichi," often develop along the trunk and branches of very old Ginkgo trees in response to traumatic injury or environmental stress. These stalactite-like growths originate from embedded axillary buds and can produce both roots and shoots when they come in contact the soil (Del Tredici, 1992).

CULTIVATION AND UTILIZATION

While Ginkgo has been cultivated in China for several thousand years, the earliest written references to the plant that have been specifically cited in the literature date back only to Song dynasty documents of the early eleventh century (Li, 1956). According to these ancient texts, the tree came from an area south of the Yangtze River, in what is now the Ningguo District of southern Anhui Province. Most of these early writers praise the Ginkgo for the unique beauty of its leaves and for its edible, and medicinally active, nuts. Contrary to numerous reports in the literature, it is these attributes, rather than any special religious significance, that probably account for the tree's rapid spread in cultivation throughout China and into Korea (Li, 1956). It should be noted, however, that the oldest Ginkgos in China are generally found growing near Daoist and Buddhist temples, and that these ancient specimens have played an important role in the preservation and dissemination of the species (Figure 6).

Ginkgo was introduced into western Japan from eastern China about eight hundred years ago. As is the case in China, the largest trees are growing in the vicinity of Buddhist or Daoist temples and shrines (Tsumura *et al.*, 1992). From Japan, Ginkgo was introduced into Europe at the Botanic Garden in Utrecht, Netherlands, about 1730, and into Kew Gardens, near London, England, around 1754. From England the tree was imported into North America in 1784 at Philadelphia, Pennsylvania (Del Tredici, 1991b).

Ornamental Uses

Ginkgo is cultivated throughout the temperate zones of the world for ornamental purposes. This includes areas with a Mediterranean-type climate as well as those

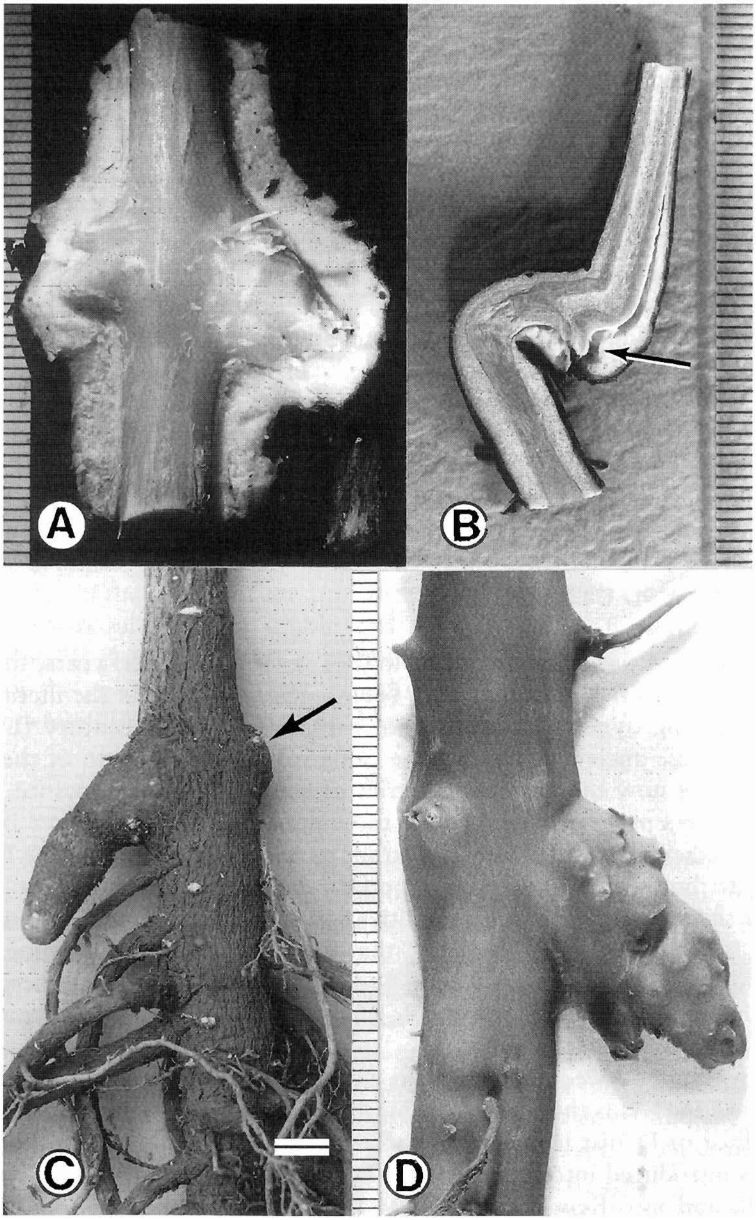

Figure 5 The early stages of lignotuber formation in two- to three-year-old Ginkgo seedlings. **A.** A partially debarked two year old seedling show the unequal development of the cotyledonary buds. Scale in millimeters. **B.** Longitudinal section of a partially debarked two-year-old seedling showing the strongly kinked stem that is often associated with lignotuber formation. Scale in millimeters. **C.** A three-year-old seedling in which one of the cotyledonary buds has formed a prominent lignotuber while the other has not (arrow). Bar equals one centimeter. **D.** A debarked three-year-old seedling showing the xylem traces of the numerous dormant shoot buds on a well-developed lignotuber. Scale in millimeters. Reprinted from Del Tredici, 1992.

Figure 6 A two thousand year-old Ginkgo growing on the grounds of an ancient temple in Xin Cun Village, Tan Chen County, Shandong Province, China. In 1985, the tree was 37 meters tall, with a trunk DBH of 2.3 meters. It is a staminate tree, with a large ovulate branch grafted onto it.

with a cold-temperate climate where minimum winter temperatures can reach –30° C. While Ginkgo grows best when planted in full sun, it shows the ability to persist indefinitely under low light and low nutrient conditions, such as when planted along the streets of densely populated cities (Handa *et al.*, 1997). In the eastern United States, Ginkgo grows rapidly within USDA hardiness zones 5 to 8, a region characterized by abundant, year-round moisture, high temperatures during the growing season, cold winters, and acid to neutral soils. Ginkgo does not perform particularly well in subtropical climates or on soils that are overly wet or dry during the growing season (Santamour *et al.*, 1983b; Del Tredici, 1991b; Liang, 1993). Relative to other commonly cultivated trees, Ginkgo possesses a high degree of resistance to insect damage and to fungal, viral, and bacterial diseases, as well as to ozone and sulfur dioxide pollution, making it an excellent choice for planting in urban areas (Sinclair *et al.*, 1987; Honda, 1997).

Numerous selections of Ginkgo have been made for ornamental purposes during its long history. Older horticultural forms that are still cultivated include: "Epiphylla" an ovulate tree which produces seeds attached to the leaves; "Fastigiata" with a narrow, upright growth habit; "Pendula" with a spreading growth habit composed entirely of horizontal branches; and "Variegata", a generally unstable form with leaves striped with yellow or white (Santamour *et al.*, 1983a). These, as well as other more recent cultivars can be propagated from rooted softwood cuttings in summer, hardwood cuttings in winter, twig grafting in late winter, or bud grafting in late summer (Del Tredici, 1991b; Liang, 1993). Because of complex epigenetic effects, however, both rooted cuttings and grafted plants generally fail to reproduce the upright form of the seed-grown parent they were propagated from. Instead, they tend to produce low-branched, vase-shaped trees that lack a dominant central leader (Figure 7) (Del Tredici, 1991b, 1991c). At the present time, fastigiate male clones are the only vegetatively propagated selections that are widely available from commercial nurseries in Europe and North America.

Seed Production

Each Ginkgo seed contains a single, thin-shelled "nut," that is traditionally consumed as both a food and a medicine throughout Asia. Dry nuts, which constitute 59% of the fresh nut weight, have a composition of roughly 6% sucrose, 68% starch, 13% protein, and 3% fat (Duke, 1989). The commercial production of Ginkgo nuts has been established in China for over 600 years, and at least 44 cultivars have been selected in that country based on the size and shape of their nuts, and on their productivity (Santamour *et al.*, 1983a; Liang, 1993; He *et al.*, 1997). These cultivars are usually propagated through grafting on seedling rootstocks, and they begin producing nuts at about 5 years of age (Figure 7). For the widely grown cultivar "Dafushon," annual yields in Jiangsu Province, China vary between 5 and 10 kilograms of nuts for 15-year-old trees and between 50 and 100 kilograms for 50-year-old trees. In general, Ginkgo produces a heavy crop of seeds every other year, with relatively light crops in alternate years (Del Tredici, 1991b; Liang, 1993). While precise figures are difficult to come by, one recent estimate of the Chinese

Figure 7 A grove of grafted Ginkgo trees cultivated for their edible nuts on Dongting Shan, Jiangsu Province, China. Note the spreading, vase-shaped form of the tree. Reprinted from Del Tredici, 1991b.

crop suggests that 700,000 to 800,000 trees produce an average of between six to seven thousand tons of dried nuts per year (He *et al.*, 1997).

Raw Ginkgo nuts, cleaned of their fleshy pulp, have long been used in traditional Chinese medicine to treat a variety of lung-related ailments such as asthma and bronchitis, as well as for the treatment of kidney and bladder disorders. They also display antibiotic effects against a variety of bacterial pathogens (Perry, 1980; Bensky and Gamble, 1986). Raw Ginkgo nuts contain a toxin that has been identified as 4-O-methylpyridoxine (MPN), whose primary mode of action is to antagonize the activity of vitamin B6 (Wada and Haga, 1997). Typically, children are much more susceptible to poisoning from Ginkgo nuts than adults.

For culinary purposes, Ginkgo seeds must be cooked to eliminate the potential for poisoning. They are usually steamed until the hard shell cracks open, allowing the kernel to be removed. In China, these kernels are either boiled in sugar water to make a sweet soup or roasted and eaten plain. Because of their potential toxicity, however, people are generally advised not to eat too many Ginkgo nuts at one sitting.

Leaf Production

Ginkgo leaves are known to contain a wide variety of medicinally active chemicals, most notably terpenoids (ginkgolides and bilobalide) and flavonoids (glycosides of kaempferol, quercetin, isorhamnetin, etc.) (Boralle *et al.*, 1988; DeFeudis, 1998). The use of Ginkgo leaf extract for pharmaceutical purposes was originally developed in Germany in 1965, and the first commercially available Ginkgo leaf extract was registered for human use in 1974 in France, under the code-name "EGb 761" (DeFeudis, 1998). This extract is made from dried Ginkgo leaves and has a standardized content of 22–27% flavonol glycosides and 5–7% terpene trilactones. This extract is taken internally for the treatment of cerebral and peripheral vascular diseases, as well as to alleviate some of the ailments associated with ageing, including dizziness, ringing in the ears, and short-term memory deterioration. So far as is known, the extract has only minimal side effects, even after prolonged use (DeFeudis, 1998; Juretzek, 1997). Contrary to numerous reports in the literature, Ginkgo leaf preparations have played a very minor role in the practice of traditional Chinese medicine, and have only recently been listed in official *Materia Medica.*

Since 1982, Ginkgo leaves have been cultivated on a large scale in both France (480 hectares) and the United States (460 hectares) specifically for the production of the EGb 761 extract. When grown for this purpose, seedlings are spaced 40 centimeters apart in rows 1 meters apart, producing a density of approximately 25,000 plants per hectare (Figure 8). Special pruning techniques are used to keep the trees below 3 meters tall, thereby allowing the use of mechanical harvesting equipment. Green leaves are generally harvested in mid- to late summer, after which the plants are cutback to near ground level once every four or five years. The new growth

Figure 8 The Ginkgo plantation in Sumter, South Carolina, in early spring. For scale, the individual segments of the irrigation system are about 45 meters long. Reprinted from Del Tredici, 1991b.

following such low cutbacks originates from buds located at the base of the stem or on basal lignotubers. When provided with an adequate supply of moisture and fertilizer during the growing season, the annual height growth from the point of cutting is typically a meter or more (Del Tredici, 1991b).

In China, yellow leaves are typically harvested at the same time that the nuts are collected, in early autumn, and sold for the manufacture of leaf extracts. These older leaves are not as rich in ginkgolides and other medicinally active compounds as green leaves, and consequently command a lower price in the international market. Since 1992, over 2000 hectares of Ginkgo seedlings have been planted in eastern China specifically for the production of green leaves. The first of these plantations began producing marketable quantities of leaves in 1996, and projections are for yields to increase dramatically over the next five to ten years (Balz, 1997; He *et al.*, 1997).

The use of Ginkgo leaf extract for therapeutic as well as other purposes has grown dramatically since its introduction in 1974. While accurate figures are difficult to come by, recent estimates of the world wide sales of Ginkgo leaf products suggest that it is around half a billion US dollars (see Warrier and Corzine, this volume), a truly remarkable figure given that the product has only been on the market for 25 years.

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