The Ethnobotany and Ethnopharmacology of Wild Tomatillos, *Physalis longifolia* Nutt., and Related *Physalis* Species: A Review¹

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The Ethnobotany and Ethnopharmacology of Wild Tomatillos, Physalis longifolia Nutt., and Related Physalis Species: A Review. The wild tomatillo, *Physalis longifolia* Nutt., and related species have been important wild-harvested foods and medicinal plants. This paper reviews their traditional use as food and medicine; it also discusses taxonomic difficulties and provides information on recent medicinal chemistry discoveries within this and related species. Subtle morphological differences recognized by taxonomists to distinguish this species from closely related taxa can be confusing to botanists and ethnobotanists, and many of these differences are not considered to be important by indigenous people. Therefore, the food and medicinal uses reported here include information for *P. longifolia*, as well as uses for several related taxa found north of Mexico. The importance of wild *Physalis* species as food is reported by many tribes, and its long history of use is evidenced by frequent discovery in archaeological sites. These plants may have been cultivated, or "tended," by Pueblo farmers and other tribes. The importance of this plant as medicine is made evident through its historical ethnobotanical use, information in recent literature on *Physalis* species pharmacology, and our Native Medicinal Plant Research Program's recent discovery of 14 new natural products, some of which have potent anti-cancer activity.

La Etnobotánica y Etnofarmacología de los Tomatillos Silvestres, Physalis longifolia Nutt., y Especies Afines a Physalis: Una Revisión. El tomatillo silvestre, *Physalis longifolia* Nutt., y especies afines han sido un importante recurso de alimentos silvestres y de plantas medicinales. Revisamos los usos tradicionales para la alimentación y la medicina, las dificultades taxonómicas, y proporcionamos los últimos descubrimientos de la química medicinal de esta y de otras especies afines. Las sutiles diferencias morfológicas reconocidas por los taxónomos para poder distinguir las estrechas relaciones de taxones entre estas especies son confusas para los botánicos y los etnobotánicos, pero estas diferencias no son reconocidas como importantes por las poblaciones nativas. Por lo tanto, los usos alimenticios y medicinales reportados incluyen no sólo información sobre *P. longifolia*, sino también para varios taxones relacionados que se encuentran al norte de México. La importancia de las especies silvestres de *Physalis* como alimento es reportada por muchas tribus y su larga historia de uso se pone de manifiesto por el descubrimiento frecuente en yacimientos arqueológicos. Estas plantas pueden haber sido cultivadas o "atendidas" por los agricultores de Pueblos y otras tribus. La importancia de esta planta como medicina se destaca por su historia de uso etnobotánico, por la literatura reciente sobre la farmacología de las especies de *Physalis* y por el descubrimiento reciente en nuestro Programa Nativo de Investigación de Plantas Medicinales de 14 nuevos productos naturales, algunos de los cuales tienen potente actividad de anti-cáncer.

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Introduction

Physalis longifolia Nutt., wild tomatillo or longleaf groundcherry, is a perennial herb that occurs throughout the continental U.S. and into southern Canada and northern Mexico (Fig. 1). Its habitat includes old fields, open woods, and prairies, but it thrives in disturbed sites, including roadsides. Plants form colonies through the spread of underground rhizomes and, because the plant is so common, it is often considered to be a weed.

The papery calyx (husk) that encloses the tasty fruit of *P. longifolia* is a distinctive characteristic of the genus *Physalis*, which includes cultivated species such as tomatillo (*P. philadelphica* Lam.) and Chinese lantern (*P. alkekengi* L.). The name *Physalis* is Greek for "a bladder," a reference to the inflated calyx. The genus *Physalis* is a member of the Nightshade family, Solanaceae, which includes tomatoes, potatoes, and tobacco. All nightshades are considered somewhat poisonous and may contain toxins in some parts of the plant. Many fruits in the Solanaceae are edible, including the ripe fruits of *P. longifolia*, although its foliage and green fruit are considered poisonous at least to livestock (Fuller and McClintock 1986; Peterson 1977).

Taxonomy

There are at least 75 known species in the genus *Physalis* (Whitson and Manos 2005). At times, species in the closely related genera of *Chamaesaracha*, *Leucophysalis*, *Margaranthus*, *Oryctes*, and *Quincula* have been included in the genus *Physalis*. *Physalis* species are annual or perennial, erect or decumbent, sometimes rhizomatous, glabrous or pubescent, and with various-ly toothed or lobed leaves. *Physalis* is believed to have originated in Mexico, and there is only one species (*P. alkekengi*) whose origin is not of the

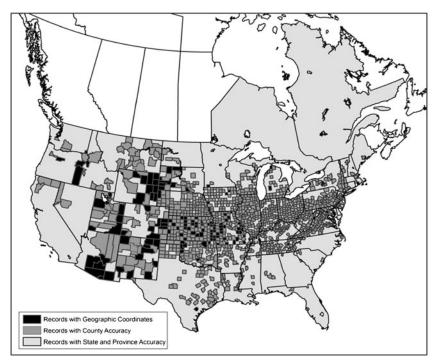


Fig. 1. Range of *Physalis longifolia* in the U.S. and Canada determined by information we obtained from 14 herbaria and other databases (references available upon request).

New World, although many cultivated and weedy *Physalis* species have been introduced, both intentionally and inadvertently, to warm areas worldwide. Whitson (2011) has proposed separating *P. alkekengi* into a new genus, *Alkekengi*, and conserving the name *Physalis* for the rest of the species. This is based on recent molecular studies that separate *Alkekengi*, in addition to its distinctive red inflated calyx, lobed white flowers, and its unique Eurasian geographic distribution.

There are 29 *Physalis* species in the United States, of which four are non-native. *Physalis longifolia* and *P. viscosa* L. are listed as noxious weeds in California, where *P. longifolia* was apparently introduced (USDA, NRCS 2011; Invasive Plant Atlas of the United States 2011).

Historically, Physalis species have been taxonomically classified based on characters such as habit, hair type, and number of calyx angles (Whitson and Manos 2005). Many species are not easily distinguished without careful examination and can be confused even by botanists. For this reason, several species have been misidentified in historical ethnobotanical accounts, as discussed below. Also, native people likely used several species interchangeably, as evidenced by the fact that indigenous names have been used for more than one species. In addition, nomenclatural changes have resulted from recent analyses using molecular data and the results of artificial hybridization, which have provided new understanding of relationships among taxa. Thus, references to some species in the older literature (e.g., P. pumila Nutt., P. lanceolata Michx., and P. virginiana Mill.) (USDA, NRCS 2011) cannot be relied upon with certainty.

The typical *Physalis* species is an herb with axillary yellow flowers that are solitary and bee pollinated (Sullivan 1984). Once pollination has occurred, the corolla drops off and the calyx expands until the developing berry is completely enveloped by a papery husk. These husked fruits are characteristic of the genus and make them easy to recognize as a group. The manyseeded berries of Physalis species range from greenish to yellow to orange and are sometimes flushed with purple or red (Whitson and Manos 2005), thus explaining the use of the common names "ground tomato" and "husk tomato" (Castetter 1935). The berry of P. longifolia is yellow-green when ripe and tastes like an effervescent, under-ripened strawberry, or, when dried, tastes like a cross between a raisin and dried cranberry.

The genus *Physalis* contains several species grown for their ornamental or edible fruits, which are eaten raw or cooked. The most commonly cultivated species in North America is the tomatillo (*P. philadelphica*), which is often cultivated for food and used in *salsa verde*. Many other species, such as the Cape gooseberry (*P. peruviana* L.) and the husk tomato or *muyaca* in South America (*P. pubescens*), L. have been cultivated and eaten for their acidulous fruit (von Mueller 1895). The Chinese lantern plant (*P. alkenkengi*, referred to above), is an ornamental species that is cultivated for its brightly colored orange-red husk.

Native American Food Use

Physalis species were used by numerous North American tribes across a large geographic region (Fig. 2). Elias Yanovsky (1936) authored the first ethnobotanical compilation of *Physalis* species and their uses by Native Americans. He listed ten species of *Physalis*, including *P. longifolia*, that were used as food. Due to nomenclatural changes, nine species are listed by Moerman (2011). However, there has been little study of the food uses in any depth. Gary Nabhan stated in his "Native Crop Diversity in Aridoamerica" that "the cultural geography of *Physalis* deserves further investigation" (Nabhan 1985). And it is clear that they were used by more tribes than we have been able to document here.

Edward Castetter (1935) reported in his "Uncultivated Native Plants Used as Food— Ethnobotanical Studies in the American Southwest" that the berries of *P. neomexicana* Rydb. and *P. longifolia* were both used as food by the Rio Grande Pueblos in New Mexico. The fruits usually were boiled but sometimes were eaten fresh. Castetter also reported that at Acoma and Laguna Pueblos, the fruits were referred to by the names *charoka* and *shuma charoka*. These species were used in a similar manner at the San Felipe Pueblo and were known as *sharoka*.

According to Matilda Stevenson's (1915) "Ethnobotany of the Zuni Indians," the berries of *P. fendleri* A. Gray (now recognized as *P. hederifolia* A. Gray by Allred 2010) had the same Zuni name (*Ke'tsitokia*, which refers to an insect that feeds upon the plant) as *P. longifolia*. This suggests that these species were not distinguished from one another and may have been used interchangeably. Stevenson reported that this plant grew wild in lowlands on the Zuni reservation in western New Mexico and was also cultivated in the small

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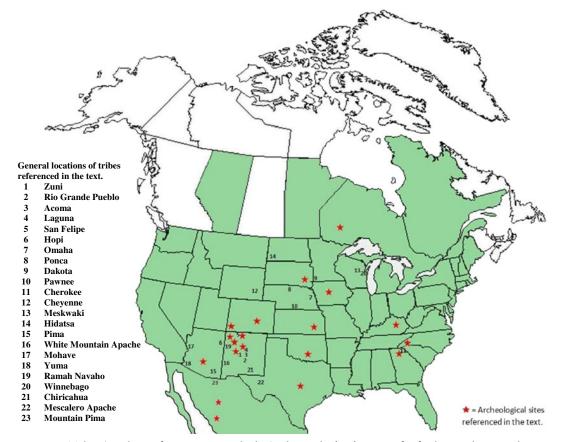


Fig. 2. Tribes (numbers refer to names on the key) who used *Physalis* species for food or medicine, and stars designate some of the archeological sites (citations in text) where *Physalis* seeds have been found. The shaded range, by state and province, for all *Physalis* species, is from the USDA Plants database (USDA NRCS 2011).

gardens worked by women. The ripe red fruits, which were described as tasting similar to a tomato, were boiled with a small amount of water and ground in a mortar with raw onions, chiles and coriander seeds. The dish was regarded as a great delicacy (Castetter 1935). Ethnologist Walter Hough (1898) also reported that the Zuni dried and ground the berries to produce a meal for making bread and stated that in the "old times" the berries of *P. longifolia* were eaten by the Hopi.

In Frank Cushing's "Zuni Breadstuffs" (based on his work on the Zuni Reservation in the 1880s), he writes: "Among the sandy defiles of the upper plains, mesas, and mountains, grow abundant low bushes bearing very juicy little yellow berries called *k'ia'-po-ti mo'-we*, or the 'juice-filled fruitage'." These berries were in high favor with the ancient Zunis as food according to Cushing. They were boiled or stewed to make a sauce, which, although not quite so acidic, otherwise tasted like cranberry sauce (Cushing 1920). The wild tomatillo is still currently used as food at the Zuni Reservation. In Rita Edaakie's "*Idonaphshe*—Let's Eat—Traditional Zuni Foods," she gives a recipe for the use of *K'e: ts'ido'kya K'yalk'osenne*, or tomatillo paste, in which the domesticated tomatillos, *P. philadelphica*, are used to make a tasty sauce that includes roasted chiles and green onions (Edaakie 1999; Nabhan 2008). This recipe is certainly an adaptation of the previous use of native *Physalis* species.

There is documented food use of seven other *Physalis* species found north of Mexico. Because these species co-occur in the region of use of *P*.

longifolia in the United States and are similar to it, they are being reported here. Melvin Gilmore reported that the fruits of *P. heterophylla* Nees were made into a sauce for food by the Omaha, Ponca, Dakota, and Pawnee. When there was sufficient quantity, the fruits were dried for the winter (Gilmore 1913). The Omaha and Ponca name, *Pe igatush*, translates as "forehead, to pop," referring to popping the inflated calyx against the head, a playful diversion that kids still shared in Nebraska when growing up in the 1970s (Kindscher, personal communication).

When the Dakota first saw figs, they likened them (likely because of their sticky texture and sweetness when dried) to Physalis, and called them Tomaniohpe washichu, "White man's Physalis" (Gilmore 1977). The Cherokee (Hamel and Chiltoskey 1975), Cheyenne (Hart 1981), and Meskwaki (Smith 1928) also used the berries of P. heterophylla as food. Buffalobird Woman (a Hidatsa), informed ethnobotanist Gilbert Wilson in 1916 that wild tomatillos were scarce on the Hidatsa reservation in North Dakota, but when they were found, the fruits were collected and eaten fresh in the field or brought back to the lodges. When occasionally found in quantity, the fruits were pounded and shaped into patties that were dried, similar to those made with chokecherries (Nickel 1974)

The bud clusters of a species identified as *P. lanceolata* were used in the spring by the Dakota as food (Gilmore 1913). Later, this tribe also ate the firm young, green "seed pods" boiled with meat. According to current taxonomic authorities, *P. lanceolata* is a species that occurs only in the Carolinas and Georgia, so Gilmore's account must actually refer to one of the perennial species —*P. virginiana, P. longifolia,* or *P. pumila.* All of these species occur in northeast Nebraska on the Dakota reservation where Gilmore interviewed elders and collected roots (see Fig. 3) but apparently did not collect a voucher specimen.

Other species used as food include *P. acutifolia* (Miers) Sandw., which the Pima in the Southwest desert ate raw (Rea 1997). *P. hederifolia* fruits were eaten by the White Mountain Apache, Mohave, and Yuma (Moerman 2011). *P. pubescens* fruit were eaten fresh, cooked, or dried by the Mohave, Yuma, and Ramah Navajo (Moerman 2011). *P. virginiana* fruit were eaten raw by the Meskwaki in Wisconsin after they were "touched by frost in the fall" (Smith 1928). This species also was reported by Huron Smith to be eaten by

the Winnebago in Wisconsin in the 1930s (Kindscher and Hurlburt 1998). The annual *P. angulata* L. fruit were eaten fresh by the Eastern Band of the Cherokee when they turned yellow (Cozzo 2004). Also, the annual *P. neomexicana* was reported by Edward Castetter in 1936 to be considered a delicacy and commonly eaten by Chiricahua and Mescalero Apache in New Mexico (Castetter and Opler 1936). Additionally, in northern Mexico, *P. caudella* Standl. (which also occurs in Arizona and New Mexico) is common in Mountain Pima agricultural fields in Chihuahua. Fruits are eaten green or ripe, primarily by children (Laferriere et al. 1991).

Ancient Uses of *Physalis* Species as Food

Physalis species occur commonly in archaeological materials in the Southwest, Great Plains, and Midwest (see Fig. 2). Identifying charred seeds to species is not possible, so they all are simply identified as *Physalis* species. The charred seeds have been found at archaeological sites in New Mexico dating from as early as AD 298 at LA 109100 on Ceja Mesa west of Albuquerque (Dello-Russo 1999) and at the Basketmaker III/ Pueblo I period (AD 650-900) at River's Edge west of the Rio Grande River and north of Corrales (Brandt 1991). The period of use extends into the Coalition and Classic periods of the Rio Grande Classification (AD 1200-1600), occurring at LA 1051 (Toll and McBride 2011), LA 2 (McBride and Smith 2011), and at Arroyo Hondo Pueblo (Wetterstrom 1986) in the Santa Fe district, as well as on the Pajarito Plateau near Los Alamos (McBride 2008). Seeds also have been found at Salmon Ruin, an ancestral Pueblo site in northwest New Mexico (Doebley 1981). At the Yellowjacket site in southwest Colorado, 800-year-old charred seeds of *Physalis* species were common in hearths and middens (Kuckelman 2003).

The plants often are associated with abandoned fields, as they flourish in disturbed, weedy habitats, but some archeologists (Yarnell 1965) suspect that wild tomatillos actually were cultivated or at least encouraged among other crops before Pueblo times. Prehistoric inhabitants probably cooked fresh fruits, dried the fruits, or ground dried seeds to cook with other foods (Wetterstrom 1986). All of these uses would provide opportunity for some seeds to be



Fig. 3. Top left: *Physalis longifolia* (wild tomatillo) in a field near Cimarron, Kansas. *Top right*: Fruits, sliced in half and dried, become chewy and sweet, although a little acidulous. *Middle left*: Roots of *P. longifolia*. The Omaha and Ponca names for *P. lanceolata*, and possibly also *P. longifolia*, has been translated as "crooked medicine," an apparent reference to the roots, which were used to treat headache and stomach trouble, and as a dressing for wounds. *Middle right*: Dried root samples of "crooked medicine," *P. lanceolata*, collected in 1927 by ethnobotanist Melvin Gilmore, archived at the Smithsonian's National Museum of the American Indian Cultural Resources Center in Suitland, MD (catalog number: 15/2097), used with permission. *Bottom left: P. longifolia* seeds as they appear under a microscope. *Bottom right*: Ripe fruits of *P. longifolia*. The fruits were eaten raw, cooked or dried by the Zuni, Hopi and other Native American tribes.

preserved, since a cook might inadvertently scatter some seeds during preparation of a sauce or other dish. The lower moisture content of dried seeds or fruits versus fresh increases the chance of being carbonized in a fire.

Further evidence of food usage is the discovery of *Physalis* seeds in coprolites (dried feces) of the agricultural Basketmaker III and Pueblo III people in the Four Corners region of

the Southwest. Given that about 10 percent of fecal samples contained *Physalis*, it is believed that the fruits were associated with agricultural crops and were a food of moderate importance (Minnis 1989).

Richard Yarnell (1965) studied archaeological sites of the Pajarito Plateau (near Los Alamos, New Mexico, at elevations from 6,100 to 6,700 feet). He commented: "Five species of Solanaceae 2012]

appear to have considerable significance in that they are highly correlated with growing at archaeological sites. These are Solanum jamesii, Solanum triflorum, Physalis neomexicana, Lycium pallidum, and Datura meteloides. Three other species, Chamaesaracha conioides, Physalis hederifolia var. cordifolia, and Solanum elaeagnifolium, are apparently of lesser significance." These species appear to be more than just weeds associated with the disturbance of archaeological sites, since ethnobotanical evidence suggests that all of them are associated with agricultural, food, and cultural practices (Yarnell 1965).

Physalis seeds are frequently found in archeological sites from the Great Plains to the eastern United States as well. They were widely available in the summer and fall in the eastern woodlands, where they have been found at several archeological sites (Scarry 2003). Wild tomatillo seeds are abundant at two winter camps of the Fort Ancient culture (1000-1750 AD) in east-central Kentucky. They were among the wild plants discovered at the Dymock sites in Ontario, which are Western Basin Younge phase sites (ca. AD 1000-1200) (Crawford and Smith 2003). Physalis seeds also were found at the Meehan-Schell site, a Late Woodland site (AD 850-1100) in Iowa along with many other native seeds, grains, and nuts (Mead 1981). In South Dakota, they were identified at the Mitchell site, an Initial Middle Missouri Complex (AD 900-1400) (Benn 1974).

Seeds were present at the Two Deer site in Kansas of the Bemis Creek Complex, Late Woodland (AD 550-1005) (Adair and Brown 1978). In south-central Oklahoma, they were identified at the Densmore site, Early Plains Village Period (AD 900–1250) (Drass 1993). They also were being used into the Protohistoric era at the Longhorn site in Texas in the early 1600s (Dering 1993a, b). Finally, Physalis seeds were found at the Recon John Shelter in southeastern Colorado, a Woodland/Early Ceramic site (15 BC-AD 1000) (Zier and Kalasz 1991). In addition to these ancient sites, archeological remains of Physalis have been found at historic period Cherokee sites at the Ravensford and Coweeta Creek sites in North Carolina and at Brasstown Valley in Georgia (Cable et al. 1997; VanDerwarker 2012).

Ethnopharmacology of *Physalis longifolia* and Other Related Species

In northeast Nebraska, the ethnobotanist Melvin Gilmore (1977) reported in 1919 that *P. lanceolata* was known by the Omaha and Ponca as *makan bashahon-shon*, "crooked medicine," apparently referring to the crooked roots of the plant. The root of this species (actually *P. longifolia*, *P. virginiana*, or *P. pumila*; see discussion above on Gilmore's identification) was used as medicine by the Omaha, Ponca, and Winnebago to treat headache and stomach trouble, and as a dressing for wounds. Alice Fletcher and Francis La Flesche (1911) reported that the Omaha Buffalo doctors used *P. viscosa* (Gilmore reported that this was actually *P. lanceolata*) roots to dress wounds.

The Lakota were reported to eat *P. heterophylla* fruits to increase the appetite (Rogers 1980). The Iroquois used the dried leaves and roots of *P. heterophylla* as a wash to treat venereal disease sores and also internally as a tea to treat stomachache after one was sick (Herrick 1995). The dried leaves and root of *P. pubescens* were used by the Navaho as a "life medicine" (Vestal 1952). The Meskwaki made an infusion of the whole plant of *P. virginiana* to treat dizziness (Smith 1928).

Many other *Physalis* species throughout the world have been used traditionally for medicine. One anti-cancer finding relates directly to the work discussed below. It is the use of a paste, extracted from the leaves and stems of *P. mimima* L. (a weedy species, most likely native to the New World tropics), which traditionally has been used in Thailand and Malaysia as a medicine to treat cancer (Lee and Houghton 2005).

Medicinal Chemistry, Anti-Cancer Studies, and Recent Discoveries

Physalis species are known to contain carbohydrates, lipids, minerals, vitamins, and phytosterols (Puente et al. 2011). They also are a major contributor of withanolide-type structures. Withanolides are classically defined as a group of C_{28} ergostane-type steroids with a C-22,26 δ -lactone group, first isolated from the genus *Withania* (Lavie et al. 1965). They are restricted to the Solanaceae family (subfamily Solanoideae), which includes the genera *Datura, Physalis*, and *Withania* (Zhang et al. 2012; Misico et al. 2011; Chen et al. 2011; Eich 2008; and Veleiro et al 2005). Withanolides have attracted substantial recent 5) interest due to their exhibition of significant in biological activities, specifically antimicrobial, wa antitumor, anti-inflammatory, immunomodulatory, and insect-antifeedant activities (Misico et al. 2011; Chen et al. 2011). The typical withanolide, the withaferin A, has been shown *in vitro* and *in vivo* to suppress the growth of an array of tumor cells, including breast, pancreatic, prostate, lung, leukemia, and head and neck squamous cell carci-

tial to inhibit tumorous cell growth. Most research on these compounds has been studies of ashwagandha, *Withania somnifera*, an important plant in Ayurvedic medicine for more than 3,000 years (Mishra et al. 2000). It has been used traditionally as a liver tonic, anti-inflammatory agent, aphrodisiac, treatment for arthritis and rheumatism, and as an adaptogen to promote overall health and longevity (Monograph 2004; Mishra et al. 2000).

noma, by inducing programmed cell death

(Samadi et al 2010)-therefore possessing poten-

As part of an ongoing study of withanolides by our group, the phytochemistry and biological activity of *P. longifolia* was evaluated for the first time (Zhang et al. 2011). Fourteen new withanolides (named withalongolides A-N), four acetylated derivatives and eight known compounds were isolated and identified from the aerial parts of this species (Zhang et al. 2011). The classically defined withanolide-type steroids isolated from *P. longifolia* have a diversity of oxygenation patterns.

Eight known compounds were also identified from *P. longifolia*, including seven withanolides (sitoindoside IX, withaferin A, 2,3-dihydro-3 β methoxywithaferin A, viscosalactone B, 2,3-dihy dro-3 β -*O*-sulfate withaferin A, 2,3-dihydrowithaferin A, and 3α , 6α -epoxy- 4β , 5β ,27-trihydroxy-1oxowitha-24-enolideJ) and a flavonoid glucoside, rutin (Zhang et al. 2011). A voucher specimen for this material was collected in Ellsworth County, Kansas, by Hillary Loring (collection number 3583) and deposited in the R.L. McGregor Herbarium at the University of Kansas.

When tested against human head and neck squamous cell carcinoma and against melanoma cell lines for their cytotoxicity, eight withanolides (including withalongolides A,B, C, D, E,G,H, sitoindoside IX, withaferin A, and 2,3-dihydro- 3β -O-sulfate withaferin A) and four acetylated derivatives showed potent cytotoxic effects against the cancer cells compared to normal fetal (MRC-

5) fibroblast control cells tested with IC₅₀ values in the range 0.067–9.3 μ M, while the other withanolides were inactive (Zhang et al. 2011). In addition, none of the withanolides demonstrated cytotoxicity in normal fibroblast cells at or below the concentrations where cancer cells demonstrated toxicity. For these reasons, there is considerable interest in these new compounds.

Other recent anti-cancer discoveries include those found in *P. angulata*, which demonstrated anti-metastatic and anti-angiogenic activity (Hsua et al. 2011). This species also was found to contain anti-proliferative withanolides, cyto-toxic against prostate cancer cells (Jin et al. 2012), and as well as Physalin B, which has anti-melanoma activity (Hsu et al. 2012). In addition, *P. minima* has been shown to have significant cytotoxic activity on human lung cancer cells (Leong et al. 2011).

Erroneous Hallucinogenic Information

The Louisiana State Act 159 (2006) treats P. subglabrata (now recognized as a variety of P. longifolia) as a hallucinogenic plant. This potential hallucinogen is listed at two popular culture web sites: Wikipedia (2011), and Erowid (2011), apparently because it is listed in this state act. We conducted extensive searches of the internet and academic search engines but could not find any information to support this claim. We contacted the state representative (now the Louisiana Commissioner of Agriculture) who sponsored the bill, and he informed us that "The Plant Kingdom and Hallucinogens" by Dr. Richard Evans Schultes (1970) was the source of information for Act 159. This law restricts cultivation and possession of 39 listed "hallucinogenic plants," including the fungi Amanita muscaria and *Psilocybe* spp., entire genera such as *Erythrina* spp. and also Salvia divinorum, Ipomoea violacea, and Solanum carolinense. However, Schultes made no mention of the genus Physalis. We have no alternative but to believe that the inclusion of P. subglabrata (P. longifolia var. subglabrata) as a hallucinogenic plants in Louisiana State Act 159 is erroneous.

Toxicity

There is little evidence of substantial toxicity in *Physalis* species. The fruits of species north of Mexico have been documented to be eaten as food. Two cases of livestock poisoning involving *P. angulata* foliage in hay or forage have been

reported for California (Fuller and McClintock 1986). However, the toxicity has not been confirmed. Overall there is little reason to consider the plants toxic, other than that they may contain solanine-type glycoalkaloids (Burrows and Tyrl 2001) present throughout most of the Solanaceae. Solanine, a chemical destroyed by heat, is reported to be in the green fruit. This may explain why the young bud clusters of the plants and some sauces were prepared by cooking. Like other members of the Solanaceae, including tomatoes and peppers, only the fruits of *Physalis* are generally consumed as food, while the foliage is considered somewhat poisonous.

Cultivation

We have found P. longifolia relatively easy to grow from seed in the greenhouse. Seedlings were transplanted to our research garden where all individuals of this perennial easily fruited the first year. The fruits are not only tasty in sauce, but also are sweet and flavorful when cut and dried. Because of their widespread use and occurrence in traditional Native American gardens, it is possible that P. longifolia and other wild tomatillos may have been cultivated. Gary Nabhan (2008) states that Physalis "grows as a weed among Tarahumara and Tepehuan fields in the Sierras (of Mexico) but also appears to have been semi-cultivated by some Pueblo, Navajo, and Hispanic gardeners of northern New Mexico." Paul Minnis surmised that it is one of the numerous species in the Southwest and adjacent Mexico that was actively managed for harvest (Minnis 2001).

Physalis longifolia was described as cultivated by Pueblo people by both Matilda Stevenson (1915), who had lived at Zuni Pueblo and observed it in their gardens, and also by Edward Castetter (1935). There is speculation—due to the discovery of an unusually large *Physalis* species seed at a Classic Period Hohokam site near Phoenix, Arizona—that *Physalis* may have been cultivated (Adams 2002; Bohrer 1991). It is possible that this large seed could have been from a cultivated variety from Mexico. Whether or not wild *Physalis* species were cultivated, it is clear that the *Physalis* fruits were widely appreciated and encouraged.

Conclusion

The wild tomatillo, *P. longifolia*, as well as other *Physalis* species, has a lengthy history of

being used as food and medicine by Native Americans. Species identifications are often difficult and confusing for both botanists and ethnobotanists, and many species were traditionally used interchangeably. Physalis seeds have been found at numerous archaeological sites, dating from the Archaic to the Classic period in the Rio Grande Valley; northern New Mexico and southwestern Colorado; through the Great Plains and the Midwest; and into Ontario, Canada. *Physalis* species have tasty fruits and likely were encouraged in agricultural fields and possibly even cultivated. Although less important than food uses, Native American medicinal uses of *Physalis* also were common. Recent work by our Native Medicinal Plant Research Program (http:// nativeplants.ku.edu/) has led to the discovery of many interesting new compounds, including withanolides, within the plant and fruit, some of which have potent anti-cancer activity. In addition, several recent studies highlight potential anti-cancer activity and other therapeutic uses of Physalis species. Based on the numerous, extensive, and long-term use of the fruits as food, it appears they are safe for consumption. Although this common plant is widely ignored and described as a weed, it was once an important plant for both food and medicine, and may be so again.

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Literature Cited

- Adair, M. J. and M. E. Brown. 1978. The Two Deer Site (14BU55): A Plains Woodland– Plains Village Transition. In Prehistory and History of the El Dorado Lake Area (Phase II). Project Report Series No. 47. Museum of Anthropology. University of Kansas. Lawrence.
- Adams, K. 2002. Archaeobotanical Studies and Paleoenvironmental Reconstructions, Gila River Indian Community, Arizona. P-MIP Technical Report No. 2002–03.
- Allred, K. 2010. Flora Neomexicana I: The vascular plants of New Mexico, an Annotated Checklist to the Names of Vascular Plants with Synonymy and Bibliography. Available: http://www.lulu.com/.
- Benn, D. W. 1974. Seed Analysis and Its Implications for an Initial Middle Missouri Site in South Dakota. Plains Anthropologist 19:55– 72.
- Bohrer, V. 1991. Recently Recognized Cultivated and Encouraged Plants Among the Hohokam. Kiva 56:227–235.
- Brandt, Carol B. 1991. The River's Edge Archaeobotanical Analysis: Patterns in Plant Refuse. Zuni Pueblo, New Mexico. Zuni Archaeology Program. Ethnobiological Technical Series 91-2.
- Burrows, G. E. and R. J. Tyrl. 2001. Toxic Plants of North America. Iowa State University Press, Ames.
- Cable, John, Lisa O'Steen, Leslie E. Raymer, Johannes H. N. Loubser, David S. Leigh, J.
 W. Joseph, Mary Beth Reed, Lotta Danielsson-Murphy, Undine McEvoy, Thaddeus Murphy, Mary Theresa Bonhage-Freund, and Deborah Wallsmith. 1997. A Picture Unsurpassed: Prehistoric and Historic Indian Settlement and Landscape, Brasstown Valley, Towns County, Georgia. Report on File at New South Associates, Georgia. Stone Mountain.
- Castetter, E. E. 1935. Uncultivated Native Plants Used as Food—Ethnobotanical Studies in the

American Southwest. New Mexico University Biological Series Bulletin 4(1).

- Castetter, E. F. and M. E. Opler. 1936. The Ethnobiology of the Chiricahua and Mescalero Apache; Ethnobiological Studies in the American Southwest: III. A. The Use Of Plants For Foods, Beverages And Narcotics. University of New Mexico 4:3–63.
- Chen, L. X., H. Hao, and F. Qiu. 2011. Natural Withanolides: an Overview. Natural Products Reports 28:705–740.
- Cozzo, D. N. 2004. Ethnobotanical Classification System and Medicinal Ethnobotany of the Eastern Band of the Cherokee Indians. Ph.D. Dissertation. Anthropology Department, University of Georgia.
- Crawford, G. W., and D. G. Smith. 2003. Paleoethnobotany in the Northeast. Pages 172-257. in P.E. Minnis, editor. People and Plants in Ancient Eastern North America. Smithsonian: Washington, D.C.
- Cushing, F. H. (1920). Zuni Breadstuff. Museum of the American Indian, Heye Foundation. New York.
- Dello-Russo, R. D. 1999. Climatic Stress in the Middle Rio Grande Valley of New Mexico: An Evaluation of Changes in Foraging Behaviors During the Late Archaic/ Basketmaker II Period. Unpublished Ph.D. dissertation. University of New Mexico. Albuquerque.
- Dering, J. P. 1993a. Plant Remains. In Data Recovery at Justiceburg Reservoir (Lake Alan Henry), Garza, and Kent Counties, Texas: Phase III, Season 2, edited by D.K. Boyd. Prewitt and Associates, Austin, Texas, 431–434.
- Dering, J. P. 1993b. Plant Remains. Pages 431– 434. in D.K. Boyd, editor. In Data Recovery at Justiceburg Reservoir (Lake Alan Henry), Garza, and Kent Counties, Texas: Phase III, Season 2. Prewitt and Associates, Texas. Austin
- Doebley, J. F. 1981. Plant Remains Recovered by Floatation from Trash at Salmon Ruin, New Mexico. Kiva 46:169–187.
- Drass, R. R. 1993. Macrobotanical Remains from Two Early Plains Village Sites in Central Oklahoma. Plains Anthropologist 38:51–64.
- Edaakie, R. 1999. *Idonaphshe*—Let's Eat— Traditional Zuni Foods. A:shiwi A:wan Museum and Heritage Center, Zuni, New Mexico. Zuni.
- Eich, E. 2008. Solanaceae and Convolvulaceae: Secondary Metabolites. Spring-Verlag, Berlin.

- Erowid 2011. From: http://www.erowid.org/ psychoactives/law/states/states_info1.shtml. Accessed November 15, 2011.
- Fletcher, A. C. and F. LaFlesche. 1911. The Omaha Tribe. Smithsonian Institution. Bureau of American Ethnology 27:76–78.
- Fuller, T. and E. McClintock. 1986. Poisonous Plants of California. University of California Press, Berkeley.
- Gilmore, M. R. 1913. Some Native Nebraska Plants with Their Uses by the Dakota. Nebraska State Historical Society 17:358–371.
- Gilmore, M. R. 1977. Uses of Plants by the Indians of the Missouri River Region. University of Nebraska Press, Lincoln.
- Hamel, P. B. and M. U. Chiltoskey. 1975. Cherokee lants: Their Uses—a 400 Year History. Herald Publishing Company, North Carolina. Sylva.
- Hart, J. A. 1981. The Ethnobotany of the Northern Cheyenne Indians of Montana. Journal of Ethnopharmacology 4:1–55.
- Herrick, J. W. 1995. Iroquois Medical Botany. Syracuse University Press, New York. Syracuse.
- Hough, W. 1898. Environmental Interrelations in Arizona. American Anthropologist 11 (5):133–155.
- Hsu, C., Y. Wua, L. Farh, Y. Dua, W. Tseng, C. Wuf, and F. Chang. 2012. Physalin B from *Physalis angulata* Triggers the NOXA-related Apoptosis Pathway of Human Melanoma A375 cells. Food and Chemical Toxicology 50:619–624.
- Hsua, Y., C. Wub, H. Changc, K. Kumara, M. Linb, C. Cheni, H. Choi, C. Huangi, C. Huangd, H. Leee, W. Hsiehf, J. Chungg, H. Wangh, and H. Yangi. 2011. Inhibitory effects of *Physalis angulata* on tumor metastasis and angiogenesis. Journal of Ethnopharmacology 135:762–771.
- Invasive Plant Atlas of the United States. 2011. From: http://www.invasive.org, Accessed July 31, 2011.
- Jin, Z., M. Mashuta, N. Stolowich, A. Vaisberg, N. Stivers, P. Bates, W. Lewis, and G. Hammond. 2012. Physangulidines A, B, and C: Three New Antiproliferative Withanolides from *Physalis angulata* L. Organic Letters 14:1230–1233.
- Kindscher, K. and D. P. Hurlburt. 1998. Huron Smith's Ethnobotany of the Hocąk (Winnebago). Economic Botany 52(4):352– 372.

- Kuckelman, Kristin A., editor. 2003. The Archaeology of Yellow Jacket Pueblo (Site 5MT5): Excavations at a Large Community Center in Southwestern Colorado. Crow Canyon Archaeological Center, Colorado. Cortez.
- Laferriere, J. E., C. W. Weber, and E. A. Kohlhepp. 1991. Use and Nutritional Composition of Some Traditional Mountain Pima Plant Foods. Journal of Ethnobiology 11:93– 114.
- Lavie, D., E. Glotter, and Y. Shvo. 1965. Constituents of *Withania somnifera* Dun. III. The Side Chain of Withaferin A. Journal of Organic Chemistry 30:1774–1778.
- Lee, C. and P. Houghton. 2005. Cytotoxicity of Plants from Malaysia and Thailand used Traditionally to Treat Cancer. Journal of Ethnopharmacology 100:237–243.
- Leong, O., T. Muhammad, and S. Sulaiman. 2011. Cytotoxic Activities of *Physalis minima* L. Chloroform Extract on Human Lung Adenocarcinoma NCI-H23 Cell Lines by Induction of Apoptosis. Evidence-based Complementary and Alternative Medicine. doi:10.1093/ecam/nep057.
- Louisiana State Act 159. 2006. From: http:// www.legis.state.la.us/billdata/stream document.asp?did=288583. Accessed August 15, 2011.
- McBride, Pamela J. 2008. Diet and Subsistence on the Pajarito Plateau: Evidence from Flotation and Vegetal Sample Analysis. In The Land Conveyance and Transfer Data Recovery Project: 7000 Years of Land Use on the Pajarito Plateau, Volume 3: Artifact and Sample. Analyses, edited by Bradley J. Vierra and Kari M. Schmidt, pp. 399–521. Los Alamos National Laboratory, Cultural Resources Report No. 273. New Mexico. Los Alamos.
- McBride, Pamela J. and Susan J. Smith. 2011. Agua Fria Schoolhouse Archaeobotanical Record. Manuscript on file, Southwest Archaeological Consultants, Santa Fe, New Mexico.
- Mead, B. 1981. Seed Analysis of the Meehan-Schell Site (13BN110), a great Oasis Site in Central Iowa. Journal of the Iowa Archeological Society 28:15–90.
- Minnis, P. E. 1989. Prehistoric Diet In The Northern Southwest: Macroplant Remains From Four Corners Feces. American Antiquity 54 (3):543–563.

- Minnis, P. E. 2001. One Possible Future of Ethnobiology. in R. Ford, editor. In Ethnobiology at the Millenium—Past Promise and Future Prospects. Museum of Anthropology. University of Michigan. Athropological Papers, Number 91.
- Mishra, L., B. B. Singh, and S. Dagenais. 2000. Scientific Basis for the Therapeutic Use of *Withania somnifera* (Ashwagandha): A Review. Alternative Medicine Review 5:334–346.
- Misico, R. I., V. E. Nicotra, J. C. Oberti, G. Barboza, R. R. Gil, and G. Burton. 2011. Withanolides and Related Steroids. Progress in the Chemical of Organic Natural Products 94:127–229.
- Moerman, D. 2011. Native American Ethnobotany, http://herb.umd.umich.edu/. Accessed November 11, 2011.
- Monograph. 2004. *Withania somnifera*. Alternative Medicine Review 9:211–214.
- Nabhan, G. 1985. Native Crop Diversity in Aridoamerica: Conservation of Regional Gene Pools. Economic Botany 39:387–399.
- Nabhan, G. 2008. Renewing America's Food Traditions: Saving and Savoring the Continent's Most Endangered Foods. Chelsea Green Publishing Company, Vermont. White River Junction.
- Nickel, R. K. 1974. Plant Resource Utilization at a Late Prehistoric Site in North-central South Dakota. Master's thesis, Department of Anthropology. University of Nebraska.
- Peterson, L. E. 1977. A Field Guide to Edible Wild Plants: Eastern and Central North America. Houghton Mifflin Company, New York.
- Puente, L. A., C. A. Pinto-Munoz, E. S. Castro, and M. Cortes. 2011. *Physalis peruviana* L., the Multiple Properties of a Highly Functional Fruit: a Review. Food Research International 44:1733–1740.
- Rea, A. M. 1997. At the Desert's Green Edge: An Ethnobotany of the Gila River Pima. University of Arizona Press, Tucson.
- Rogers, D. J. 1980. Lakota Names and Traditional Uses of Native Plants by *Sicangu* (Brule) People in the Rosebud Area, South Dakota. The Rosebud Educational Society, Inc, St. Francis.
- Samadi, A. K., X. Q. Tong, R. Mukerji, H. P. Zhang, B. N. Timmermann, and M. S. Cohen. 2010. Withaferin A, a Cytotoxic Steroid from Vassobia breviflora, Induces Apoptosis in Human Head and Neck Squamous Cell Carcinoma. Journal of Natural Products 73:1476–1481.

- Scarry, C. M. 2003. Patterns of Wild Plant Utilization in the Prehistoric Eastern Woodlands. In People and Plants in Ancient Eastern North America. Smithsonian, Washington, DC: 50–104.
- Schultes, R. E. 1970. The Plant Kingdom and Hallucinogens (part 3). Bulletin on Narcotics 22:25–53.
- Smith, H. H. 1928. Ethnobotany of the Meskwaki Indians. Bulletin of the Public Museum of the City of Milwaukee 4(2):175–326.
- Stevenson, M. C. 1915. Ethnobotany of the Zuni Indians: Medical Practices and Medicinal Plants. Thirtieth Annual Report of the Bureau of American Ethnology 30:39–64.
- Sullivan, J. R. 1984. Pollination Biology of *Physalis viscosa* var. *cinerascens* (Solanaceae). American Journal of Botany 71:815–820.
- Toll, Mollie S., and Pamela J. McBride. 2011. Flotation Remains from Prehistoric Proveniences. Ch. 13 in Archaeological Excavations at El Pueblo de Santa Fe (LA 1051). Volume 1: Village of the Shell Bead Water People: A Prehistoric Trade and Ceremonial Community in Downtown Santa Fe, New Mexico, by Stephen C. Lentz, Archaeology Notes 410. Museum of New Mexico, Office of Archaeological Studies. Santa Fe.
- USDA, NRCS. 2011. The PLANTS Database (http://plants.usda.gov, 16 August 2011). National Plant Data Team, Greensboro, North Carolina 27401-4901 USA.
- VanDerwarker, Amber. 2012. personal communication.
- Veleiro, A. S., J. C. Oberti, and G. Burton. 2005. Chemistry and Bioactivity of Withanolides from South American *Solanaceae*. in Atta-ur-Rahman, editor. Studies in Natural Products Chemistry. Elsevier Science, B.V.: Amsterdam, Vol. 32:1019–1051.
- Vestal, P. A. 1952. Ethnobotany of the Ramah Navaho. Papers of the Peabody Museum of American Archaeology and Ethnology. Harvard University Reports of the Ramah Project, vol 40, number 4.
- Von Mueller, B. F. 1895. Select Extra-Tropical Plants, Readily Eligible for Industrial, Culture or Naturalisation. Robert Drain, Government Printer, Melbourne, Australia.
- Wetterstrom, W. 1986. Food, Diet, and Population at Prehistoric Arroyo Hondo Pueblo, New Mexico. School of American Research Press, Santa Fe.

- Whitson, M. 2011. (2016) Proposal to Conserve the Name *Physalis* (*Solanaceae*) with a conserved type. Taxon 60:608–609.
- Whitson, M., and P. S. Manos. 2005. Untangling *Physalis (Solanaceae)* from the Physaloids: A Two-Gene Phylogeny of the Physalinae. Systematic Botany 30(1):216–230.
- Wikipedia. 2011. From: http://en.wikipedia.org/ wiki/*Physalis*. Accessed August 15, 2011.
- Yanovsky, E. 1936. Food Plants of the North American Indians. United States Department of Agriculture Miscellaneous Publication 237:1–83.
- Yarnell, R. A. 1965. Implications of Distinctive Flora on Pueblo Ruins. American Anthropologist 67(3):662–674.
- Zhang, H., A. K. Samadi, R. J. Gallagher, J. J. Araya, X. Tong, V. W. Day, M. S. Cohen, K. Kindscher, R. Gollapudi, and B. N. Timmermann. 2011. Cytotoxic Withanolide Constituents of *Physalis longifolia*. Journal of Natural Products. 74:2532– 2544.
- Zhang, H., A. K. Samadi, M. S. Cohen, and B. N. Timmermann. 2012. Antiproliferative Withanolides from the Solanaceae: A Structure-activity Study. Pure Applied Chemistry 84(6):1353–1367.
- Zier, C. J. and S. M. Kalasz. 1991. Recon John Shelter and the Archaic-Woodland Transition in Southeastern Colorado. Plains Anthropologist 36:111–138.

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