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The genus *Lycium* as food and medicine: A botanical, ethnobotanical and historical review



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ABSTRACT

Ethnopharmacological relevance: Lycium is widely distributed in the arid to semi-arid environments of North and South America, Africa, and Eurasia. In recent years, Lycium barbarum and L. chinense have been advertised as "superfood" with healthy properties. Despite of its popularity, there is a lack of an integrated and critical appraisal of the existing evidence for the use of Lycium.

Aim of the study: There is a need to understand: 1) Which species were used and how the uses of Lycium developed spatially and over time, 2) how uses differ among regions with different culture backgrounds, and 3) how traditional and current therapeutic and preventive health claims correlate with pharmacological findings. Methods: Information was retrieved from floras, taxonomic, botanical, and ethnobotanical databases, research articles, recent editions of historical Chinese herbals over the last 2000 years, and pharmacopoeias. Results: Of totally 97 species, 35 have recorded uses as food and/or medicine worldwide. Usually the fruits are used. While 85% of the Lycium species occur in the Americas and Africa, 26% of them are used, but 9 out of 14 species in Eurasia. In China, seven species and two varieties of the genus Lycium occur, of which four species have been used by different ethnic groups. Only L. barbarum and L. chinense have been transformed into globally traded commodities. In China, based on the name "村元", their use can be traced back over the last two mil-lennia. Lycium fruits for anti-aging, improving eyesight and nourishment were documented already in 500 C.E.(Mingyi Bielu). Recent findings explain the pharmacological foundations of the traditional uses. Especially polysaccharides, zeaxanthin dipalmitate, vitamins, betaine, and mixed extracts were reported to be responsible for anti-aging, improving eyesight, and anti-fatigue effects.

Conclusions: The integration of historical, ethnobotanical, botanical, phytochemical and pharmacological data has enabled a detailed understanding of *Lycium* and its wider potential. It highlights that the focus so far has only been on two species and that the genus can potentially yield a wide range of other products with different properties.

1. Introduction

Plant-based products are important sources of both food and medicine. Whether a plant is used as food or medicine depends on a wide range of factors, but is not necessarily intrinsic to its pharmacological or nutritional properties (Leonti, 2011; Jennings et al., 2015). In the last decades the variety of consumed crops has increased globally, especially of local agricultural varieties and species collected from the wild. These are becoming more important for human nutrition and for medicinal uses (Heywood, 2011). This increase is often based on traditional knowledge, which is defined as knowledge innovations and practices of indigenous and local communities embodying traditional lifestyles relevant for the conservation and sustainable use of biological

diversity (Xue, 2011). Traditional knowledge on plants can be used as a starting point to develop new medicines, e.g., the discovery of artemisinin (Tu, 2015), while it should be protected subject to the Nagoya Protocol (Ngo et al., 2013; Buch and Hamilton, 2011). Therefore, traditional knowledge on plants continues to play an important role in human lives for both food and medical purposes.

The fruit, leaf, root bark, and young shoot of many species of the genus *Lycium* L. have long been used as local foods and/or medicines. Recently, *Lycium* fruits, known as goji or wolfberry, have become increasingly popular in the western world because of their nutritional properties (Qian et al., 2017; Amagase, 2010; Potterat, 2010; Amagase and Farnsworth, 2011); they are even advertised as "superfood" in Europe and North America (Wolfe, 2010; Chang and So, 2015).

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Table 1
Data sources used.

Themes	Data sources	Key words
Taxonomy & Systematics	The Plant List (2013), http://www.theplantlist.org/; GBIF (Global Biodiversity Information Facility), 2017, https://demo.gbif.org/; IPNI (The International Plant Names Index), 2015, http://www.ipni.org/; LycieaeWeb (2017), http://jsmiller.people.amherst.edu/LycieaeWeb/Project_Lycieae.html; African Plant Database (version 3.4.0), 2017. http://www.ville-ge.ch/musinfo/bd/cjb/africa/; EuroPlusMed PlantBase (2011), http://ww2.bgbm.org/; eFloras (2017). http://www.efloras.org; Flora of China (Vol. 17), 1994. http://foc.eflora.cn/; Flora of China (Vol. 67), 1994; Flora of Victoria, 2015, https://vicflora.rbg.vic.gov.au/; Neotropical Flora (2017), http://hasbrouck.asu.edu/neotrop/plantae/index.php; Flora of Israel (2017), http://flora.org.il/plants/; Flora of Pakistan, 1980; Flora of the great plains, 1986; Flora of North America (2009), http://luirig.altervista.org/flora/taxa/north-america.php; NPGS (National Plant Germplasm System), 2016. https://npgsweb.ars-grin.gov/; Flora of Argentina (1992). http://www.floraargentina.edu.ar/; and scientific articles of Google scholar, science direct, web of science, NCBI (National Center for Biotechnology Information), and NEBIS (Network of Libraries and Information Centers in Switzerland).	Lycium, and the specific species names.
Traditional uses globally	Dr. Duke's Phytochemical and Ethnobotanical Databases, 1992–2016, http://phytochem.nal.usda.gov/; NPGS (National Plant Germplasm System), 2016. https://npgsweb.ars-grin.gov/; FEIS (Fire Effects Information System), 2016, http://www.feis-crs.org/feis/; NAEB (Native American Ethnobotany Database), 2003. http://naeb.brit.org/; PFAF (Plants for a Future), 2016, http://www.pfaf.org/; ETHMEDmmm (The Data Base of Ethno-medicines in the world), 2016, http://ethmed.u-toyama.ac.jp; Medicinal Plant Names Services (2017) (http://mpns.kew.org); and scientific articles of Google scholar, science direct, web of science, NCBI (National Center for Biotechnology Information), and NEBIS (Network of Libraries and Information Centers in Switzerland).	Lycium, the specific species names, Traditional use, food, medicine, ethnobotanical survey.
Use history in Chinese medicine	Chinese herbals and agronomy monographs (from ca. C.E. 100–2006; see S1); regional books of ethnobotany and herbal medicine in China. (Search with" nationality + 医药" in google book (https://books.google.com/).	"杞","地骨皮"
Pharmacopoeias	Chinese Pharmacopoeia (2015, vol. 1), European Pharmacopoeia (9.0), Japanese Pharmacopoeia (16th), Korean Pharmacopoeia (9th), Taiwan TCM Pharmacopoeia (2013), Vietnam Pharmacopoeia (4th), Ayurveda API (Vol. 6); all editions of Chinese Pharmacopoeia (1953–2015) British Pharmacopoeia Commision (2017).	Lycium

Phytochemical studies indicate that the richness in numerous constitutions of different classes, such as polysaccharides, carotenoids, flavonoids, alkaloids, amides, terpenoids, and so on, endows *Lycium* species with a variety of biological activities (Qian et al., 2017; Yao et al., 2011). Also, pharmacopoeias adopted the most popular species, *L. barbarum* and/or *L. chinense*, as herbal medicines (Wagner et al., 2011).

Thus, species of the genus *Lycium* serve as widely used source of food and medicine. Despite of its popularity, there is a lack of an integrated and critical appraisal of the existing evidence for the use of *Lycium*. From a botanical and ethnopharmacological perspective, there is a need to understand: 1) Which species were used and how the uses of *Lycium* developed spatially and over time, 2) how uses differ among regions with different culture backgrounds, and 3) how traditional and current therapeutic and preventive health claims correlate with pharmacological findings.

To answer these questions we started with a botanical overview of the genus and its accepted species, and did a comprehensive study and analysis of a large body of literature and databases.

2. Methods

Overall, information was obtained from floras, taxonomic, botanical, and ethnobotanical databases, research articles, recent editions of historical Chinese herbals, and pharmacopoeias. All sources used to extract information as well as the applied keywords are given in Table 1.

For species names and synonyms we relied on The Plant List (2013) and local floras. Distribution data and biogeographic information were obtained from IPNI (2015), GBIF (2017), LycieaeWeb (2017) and research articles. Morphological characters were extracted from the regional floras and type specimens in the Chinese National Herbarium (PE) were consulted for verification.

To gather information about the use of *Lycium* species at a global level, the following strategy was used: 1) "*Lycium*" was used as key word to search within the ethnobotanical databases (Table 1). 2) In google scholar, "*Lycium*" and "traditional" or "ethnobotany" or "medicine" or "food" or "herb" were searched. 3) The validated species

names were searched within the ethnobotanical databases and google scholar. And 4) the words "ethnobotanical survey" were searched, then "Lycium" was searched in the texts. 5) "Lycium" was also searched in regional ethnobotanical and herbal medicine monographs. Results were integrated with species data.

For the history of *Lycium*'s use we focused on China, both because a continuous documentation over the last two millennia is available, and the current boom of goji use originated in China. We relied on modern translations of classical Chinese herbals. At least one herbal per dynasty was included. If several contemporary herbals existed, the most comprehensive one and herbals adding new information were used. In total, 32 herbals from ca. C.E. 100–2006 were considered.

In order to find scientific evidence for traditional uses, we did a literature search on the phytochemistry and pharmacology of *Lycium* species. The main bioactivities and the related compounds or extracts were listed in one table.

To compare *Lycium* records in pharmacopoeias of different regions, "*Lycium*" was searched in the pharmacopoeias listed in the Index of the World Pharmacopoeias and Pharmacopoeial Authorities (document QAS/11.453/ Rev.6) published by WHO in 2016. *Lycium* was only found in the pharmacopoeias of seven Asian countries and regions.

In order to study the change of the records over time, all editions (from 1953 to 2015) of the Chinese pharmacopoeia were consulted.

Additionally, all the parameters for *Lycium* fruit and *Lycium* root included in the pharmacopoeias were extracted and analyzed with a cluster analysis to understand the relationships among pharmacopoeias. R and the package "ape" was employed (R Core Team, 2017; Paradis et al., 2004) for cluster analysis.

3. Results

3.1. Botany

The genus *Lycium* (Solanaceae) widely grows in arid to semi-arid environments of the temperate zones (Fukuda, 2001; Miller et al., 2011;

 Table 2

 The distribution of Lycium species and their uses as food and medicine.

Species name	Distribution	Food use	Medicine use	References ^a for plant uses	
L. acutifolium E. Mey. ex Dunal	South Africa, Madagascar, Lesotho	Starch of root recommended as famine food for extending bread	Pounded bark to keep a person in good health	USDA (1992–2016); Dhar et al. (2011); Watt and Warmelo (1930); Lev and Amar (2006); MPNS, 2017	
		flour; bark as condiment.			
L. afrum L.	South Africa, France, Tunisia, Sweden, Germany, Netherlands, medieval Cairo			USDA, 1992–2016; PFAF (2016); Middleditch (2012); Lev and Amar (2006); MPNS, 2017	
L. ameghinoi Speg.	Argentina	NM (not mentioned)	NM	-	
americanum Jacq.	Bahamas; Cuba; Haiti; Dominican Republic; Islas de Barlovento; Venezuela; Colombia; Costa Rica; Ecuador; Peru; Bolivia; Paraguay; Argentina	fruit as food	NM	Arenas and Scarpa (2007)	
L. amoenum Dammer	South Africa, Namibia	NM	NM	-	
L. anatolicum A.Baytop & R.R.Mill	Turkey, Armenia	NM	NM	-	
L. andersonii A. Gray	US, Mexico	Fruit as food	NM	NAEB (2003); PFAF (2016); Saunders (1920); Crosswhite (1981); Hodgson (2001); Newton (2013)	
L. andersonii var. deserticola (C.L. Hitchc.) Jeps.	US, Mexico	NM	NM	-	
L. arenicolum Miers	South Africa, Lesotho, Botswana, United States	NM	NM	-	
L. athium Bernardello	Argentina	NM	NM	_	
L. australe F.Muell.	Australia	Fruit as food	NM	PFAF (2016); Jeanes (1999); Clarke (1998)	
L. barbarum L.	Widely distributed in Asia, Europe, North America, and Austria; also appears in Africa and South America	Fruit, shoot, leaf as food	Fruit, root, leaf, calyx, bark, and whole plant as medicines for a variety of diseases	USDA, 1992–2016; PFAF (2016); Lim (2012); Liu et al. (2004 Li et al. (2001); Ali (1964); ETHMEDmm, 2016; Koleva et al. (2015); Duke (2002); Deeb et al. (2013); MPNS, 2017;	
			•	Quattrocchi (2012)	
L. berberioides Correll	US	NM	NM	<u>-</u>	
L. berlandieri Dunal	US, Mexico, Germany	Fruit as food	Plant as medicine	FEIS (2016); PFAF (2016); Kearney et al. (1960); Powell, 198 Newton (2013)	
L. berlandieri var. parviflorum (A. Gray) A. Terracc.	US, Mexico	Fruit as food	Plant as medicine	Hodgson (2001)	
L. bosciifolium Schinz	Namibia, South Africa, Botswana, Angola, Zimbabwe	Leaf as food	NM	Ndithia and Perrin, 2006	
L. brevipes Benth.	US, Mexico	NM	NM	-	
californicum A. Gray	US, Mexico, Jamaica	NM	NM	-	
L. carinatum S. Watson	Mexico, Jamaica	NM	NM	-	
L. carolinianum Walter	US, Mexico, Cuba, Easter Island, West Indies	fruit as food	NM	PFAF (2016)	
L. carolinianum var. quadrifidum (Moc. & Sessé ex Dunal) C.L. Hitchc.		NM	NM	-	
cestroides Schltdl.	Argentina, Bolivia, Uruguay, Brazil, Australia, Germany, UK	NM	Analgesic	Rondina et al. (2008); MPNS, 2017	
L. chanar Phil.	Argentina, Bolivia, Chile	NM	NM	-	
chilense Bertero	Argentina, Chile, Paraguay, Bolivia, UK, Brazil, Switzerland, Ecuador, France	NM	Fruit as medicine	NPGS (2016); USDA, 1992–2016	
L. chinense Mill.	Widely distributed in Asia, Europe, North America, and Austria	Fruit, leaf and young shoot as food; seed for coffee; leaf as tea	Fruit, root, leaf, bark, and whole plant as medicines	NPGS (2016); PFAF (2016); USDA, 1992–2016; Lim (2012); ETHMEDmm, 2016; MPNS,2017; Duke (2002); Quattrocchi (2012)	
L. chinense var. potaninii (Pojark.) A.M.Lu	China	NM	Root bark as medicine	Li et al. (2001)	
L. ciliatum Schltdl.	Argentina, Brazil, Bolivia	NM	Leaf as medicine for digestive and stomach inflammations	Trillo et al. (2010); Toledo et al. (2014)	
L. cinereum Thunb.	South Africa, Botswana, Namibia, Lesotho	Fruit as food	Treat headache and rheumatism; root: anodyne, kidney disease, perfume	Iwu (2014); Dhar et al. (2011); Van Damme (1998); MPNS, 2017	
L. cooperi A. Gray	Mexico, US	NM	NM	_	
L. cuneatum Dammer	Argentina, Paraguay, Bolivia	NM	NM	_	
L. cyathiformum C.L. Hitchc.	Bolivia, Argentina	NM	NM		
s. cyanajormani G.E. HHCHC.	Donviu, mgemma	17171	17171	(continued on next p	

Species name Distribution Food use Medicine use References^a for plant uses

Species name	Distribution	Food use	Medicine use	References ^a for plant uses	
L. cylindricum Kuang & A. M. Lu	China	NM	NM	-	
L. dasystemum Pojark.	China, Iran	Fruit as food	Fruit as medicine	Ali (1980); Azadi et al. (2007); Li et al. (2001);	
L. decumbens Welw. ex Hiern	South Africa, Namibia, Angola	NM	NM	-	
L. densifolium Wiggins	Mexico	NM	NM		
L. depressum Stocks	Iran, Russia, Israel, Turkmenistan, Iraq, Palestinian Territory, Afghanistan, Turkey, Pakistan, Jordan	NM	Leaf and fruit for kidney problems	Tabaraki et al. (2013); Ghasemi et al. (2013)	
L. deserti Phil.	Chile	NM	NM	_	
L. dispermum Wiggins	Mexico	NM	NM	_	
L. distichum Meyen	Peru, Bolivia, Chile	NM	NM	_	
L. divaricatum Rusby	Peru, Bolivia	NM	NM	_	
L. edgeworthii Miers	India, Pakistan, Iran	NM	NM	_	
L. eenii S. Moore	Namibia	NM	NM	_	
L. elongatum Miers	Argentina	NM	Leaf for digestive	Toledo et al., 2014; Trillo et al., 2010.	
L. europaeum L.	Spain, France, Israel, Palestinian Territory, Algeria, Portugal, India, Tunisia, Egypt	Fruit and young shoot as food	Fruit, leaf, bark, and whole plant are used for a variety of treatments	PFAF (2016); Fratkin (1996); Dafni and Yaniv (1994); Said et al. (2002); El Hamrouni, 2001; Boullard (2001); Pieroni et al. (2002); Al-Quran (2007); El-Mokasabi (2014); Turker et al. (2012); Leporatti and Ghedira (2009); Licata et al. (2016); MPNS, 2017	
L. exsertum A. Gray	US, Mexico	Fruit as food	NM	NAEB (2003); Hodgson (2001); Newton (2013); Nabhan et al.	
L. ferocissimum Miers	Australia, South Africa, New Zealand, Morocco, Namibia, US, Lesotho, Spain, Norfolk Island, Tunisia	Fruit as food	Plant for detoxication of narcotic poisoning	(1982) Watt and Breyer-Brandwijk (1962); Arnold et al. (2002); MPNS, 2017	
L. fremontii A. Gray	US, Mexico	Fruit as food	NM	NAEB (2003); PFAF (2016); Watt and Breyer-Brandwijk (1962); MPNS, 2017	
L. fuscum Miers	Argentina	NM	NM	_	
L. gariepense A.M.Venter	South Africa, Namibia	NM	NM	_	
L. gilliesianum Miers	Argentina, Chile	NM	NM	_	
L. glomeratum Sendtn.	Argentina, Paraguay, Bolivia, Brazil, China	NM	NM	_	
L. grandicalyx Joubert & Venter	South Africa, Namibia	NM	NM	_	
L. hantamense A.M.Venter	South Africa	NM	NM	_	
L. hassei Greene	US	NM	NM	_	
L. hirsutum Dunal	South Africa, Namibia, Botswana	NM	NM		
L. horridum Thunb.	South Africa, Namibia, Botswana South Africa, Namibia, Madagascar, Botswana, Lesotho, Angola, Iran, Mauritius, Turkey	NM	NM	-	
L. humile Phil.	Chile, Argentina	NM	NM	_	
L. infaustum Miers	Argentina, Colombia, Bolivia, Ecuador, Dominican, Turks And Caicos Islands, Jamaica, Peru, Portugal, Paraguay	NM	NM	-	
L. intricatum Boiss.	Spain, Morocco, Portugal, Mauritania, Algeria, Egypt, Saudi Arabia, Tunisia, Tunisia, Italy	NM	Seed: helminthiasis, digestive; fruit: eye diseases	Abouri et al. (2012); Ouhaddou,. et al. (2014); Boulila and Bejaoui (2015); Abdennacer et al. (2015); MPNS, 2017	
L. isthmense F. Chiang	Mexico	NM	NM	=	
L. leiostemum Wedd.	Chile, Peru, Mexico	NM	NM	_	
L. macrodon A. Gray	US, Mexico	NM	NM	_	
L. makranicum Schonebeck-Temesy	Pakistan	NM	NM	_	
L. martii Sendtn.	Brazil, Cuba	NM	NM	_	
L. mascarenense A.M. Venter & A.J. Scott	Mauritius, Madagascar, South Africa, Mozambique,	NM	NM	_	
L. mascarenense A.ivi. Venter & A.J. Scott	Reunion	INIVI	INIVI	-	
L. megacarpum Wiggins	Mexico	NM	NM	-	
L. minimum C.L. Hitchc.	Ecuador	NM	NM	-	
L. minutifolium Remy	Chile, Argentina, Mauritius	NM	NM	-	
L. morongii Britton	Argentina, Paraguay, Bolivia	NM	NM	_	
L. nodosum Miers	Argentina, Mexico, Paraguay, Ecuador, Venezuela, Bolivia, Peru	NM	NM	-	
L. oxycarpum Dunal	South Africa, Namibia, Angola, US	NM	Used as medicine, no details	Arnold et al. (2002); MPNS, 2017 (continued on next page	

Table 2 (continued)

Species name	Distribution	Food use	Medicine use	References ^a for plant uses
L. pallidum Miers	US, Mexico	Fruit as food	Plant and root as medicine, for toothache and chickenpox	NAEB (2003); FEIS (2016); PFAF (2016); Kindscher et al. (2012); Saunders (1920); McClendon (1921); Powell (1988); Vines (1960); Hodgson (2001); Middleditch (2012); MPNS, 2017; Quattrocchi (2012)
L. parishii A. Gray	US, Mexico	Fruit as food	NM	Nabhan et al. (1982); Hodgson (2001)
L. parishii var. modestum (I.M. Johnst.) F. Chiang	Mexico	NM	NM	-
L. petraeum Feinbrun	Italy, Jordan; EuroPlusMed PlantBase	NM	NM	-
L. pilifolium C.H. Wright	South Africa, Namibia, Botswana	NM	NM	_
L. prunus-spinosa Dunal	South Africa, Namibia	NM	Used as medicine, no details	Arnold et al. (2002); MPNS, 2017
L. puberulum A. Gray	US, Mexico	NM	NM	-
L. pubitubum C.L.Hitchc.	US, Mexico	NM	NM	_
L. pumilum Dammer	South Africa, Namibia	NM	NM	_
L. rachidocladum Dunal	Chile	NM	NM	-
L. repens Speg.	Argentina, US	NM	NM	-
L. richii A. Gray	US, Mexico	Fruit as food	NM	Watson (1888); Hodgson (2001)
L. ruthenicum Murray	China, Iran, Afghanistan, India, Mexico, Pakistan, Russian, Turkmenistan, Georgia	Fruit as food	Fruit: ophthalmic, blindness (veterinary); leaf: remove blocked	USDA (, 1992-, 2016); PFAF (2016); Ballabh et al. (2008); Gairola et al. (2014); MPNS, 2017
	v1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	n	urine; diuretic	PRAT (0016) AF 111 1: 1 (0010)
L. sandwicense A. Gray	Islands across the Pacific (Easter Island, Hawaiian Islands, Ogasawara Islands and Daitou Island)	Fruit as food	NM	PFAF (2016); Middleditch (2012)
L. schizocalyx C.H. Wright	South Africa, Botswana, Namibia, Mozambique	NM	NM	-
L. schreiteri F.A.Barkley	Argentina	NM	NM	
L. schweinfurthii Dammer	Spain, Israel, Morocco, Greece, Portugal, Algeria, Egypt, Tunisia, Mauritania, Cyprus	NM	Leaf and fruit are used for stomach ulcer	PFAF (2016); Auda (2011); Jamous et al. (2015)
L. shawii Roem. & Schult.	Israel, Palestinian Territory, Saudi Arabia, Ethiopia, Oman, Egypt, Jordan, South Africa, Botswana, Yemen	Fruit and young shoot as food	Leaf, fruit, aerial part, and stem are used for a variety of treatments	Seifu (2004); Soltan and Zaki (2009); Cherouana et al. (2013); Ghazanfar (1994); Hassan-Abdallah et al. (2013); Trabsa et al. (2015); Chermat and Gharzouli (2015); Alkuwari et al. (2012); Sher and Alyemeni (2011); Gaweesh et al. (2015); Iwu (2014); MPNS, 2017; El-Ghazali et al. (2010); Molla et al. (2011); Dahech et al. (2013)
L. shockleyi A. Gray	US, Mexico	NM	NM	_
L. stenophyllum J. Rémy	Chile, Peru, Argentina	NM	NM	_
L. strandveldense A.M. Venter	South Africa	NM	NM	-
L. tenuispinosum S.B. Jones & W.Z. Faust	Argentina, Chile, Paraguay	NM	NM	-
L. tenuispinosum var. friesii (Dammer)C.H. Hitchc.	Argentina	NM	NM	-
L. tetrandrum Thunb.	Namibia, South Africa, Angola	Fruit as food	NM	Watt and Breyer-Brandwijk (1962); MPNS, 2017
L. texanum Correll	US, Mexico	NM	NM	-
L. torreyi A. Gray	US, Mexico	Fruit as food	Whole plant and root as medicine, for chickenpox and toothache	NAEB (2003); FEIS (2016); Kearney et al. (1960); Powell (1988); Vines (1960); Hodgson (2001); MPNS, 2017; Quattrocchi (2012)
L. truncatum Y.C. Wang	China	NM	Root bark as medicine digupi	Li et al. (2001)
L. tweedianum Griseb.	Colombia, Ecuador, Dominican, Tuks And Caicos Islands, Jamaica, Bolivia, Bahamas, Cuba, Paraguay, Virgin Island	Fruit as food	NM	Roth and Lindorf (2002)
L. verrucosum Eastw.	US	NM	NM	-
L. villosum Schinz	South Africa, Namibia, Botswana	NM	NM	-
L. vimineum Miers	Argentina, Uruguay	NM	NM	-
L. yunnanense Kuang & A.M. Lu	China	NM	NM	-

a Species distribution and valid plant name information sources are not included, which are extracted from: The plant list (2013); IPNI (2015); GBIF (2017); eFloras (2017); African Plant Database (Conservatory and Botanical Garden of Geneva and South African National Biodiversity Institute), 2017; EuroPlusMed PlantBase (2011); Flora of North America (2009); VicFlora (2015); Flora of Argentina (1992); Flora of Israel (2017); Flora of China (1994). If no sources are given, no references for this species' food or medicine uses.

 ${\bf Table~3} \\ {\bf Main~morphological~characters~of~commonly~used~\it Lycium~species~of~all~continents.}$

Species	Berry	Flower	Stem and leaf
L. ruthenicum Murray	Purple-black, globose, or emarginate. Seeds brown.	Pedicel 5–10 mm. Calyx narrowly campanulate, 4–5 mm, regularly 2–4-lobed, lobes sparsely ciliate. Corolla pale purple, funnel form, ca. 1.2 cm; lobes oblong ovate, 1/3-1/2 as long as corolla tube, not ciliate.	0.2–1 m tall. Stems much branched. Leaves subsessile, solitary on young branches, leaf blade grayish, succulent, linear or sub-cylindric, rarely linear-oblanceolate,
L. truncatum Y.C. Wang	Red or orange-yellow. Oblong or oblong- ovoid, mucronated. Seeds orange.	Pedicel 1–1.5 cm. Calyx campanulate, 3–4 \times 3 mm, 2- or 3- lobed or truncate, sometimes circumscissile and only base persistent. Corolla purple or reddish purple, tube ca. 8 mm; lobes	1–1.5 m tall, sparingly armed. Branches flexible. Leaves solitary on long shoots, clustered on short shoots; leaf blade linear-lanceolate or lanceolate.
L. dasystemum Pojark.	Red, ovoid, or oblong.	ca. 4 mm, not ciliate. Pedicel 1–1.8 cm.	ca. 1.5 m tall. Stems much branched; branches grayish white, yellowish, or rarely brown-red, stout, young branches slender, elongate.
	Seeds more than 20.	Calyx campanulate, ca. 4 mm, often 2- or 3-divided halfway. Corolla purple, funnelform, 0.9–1.3 cm; tube sparingly villous inside; lobes ovate, half as long as corolla tube, ciliolate.	Leaf blade lanceolate, oblanceolate, or broadly lanceolate.
L. barbarum L.	Red or orange-yellow, oblong or ovoid,. Seeds usually 4–20, brown-yellow, ca. 2 mm.	Pedicel 1–2 cm. Calyx campanulate, 4–5 mm, usually 2-lobed, lobes 2- or 3-toothed at apex.	0.8–2 m tall. Stems and branches glabrous, branches thorny.
L. cylindricum	Berry ovoid. Seeds few.	Corolla purple, funnelform; tube8-10 mm, obviously longer than limb and lobes; lobes 5–6 mm, spreading, margin glabrescent. Pedicel ca.1 cm.	Leaves solitary or fasciculate, lanceolate or long elliptic Branches inflexed, with thorns 1–3 cm.
Kuang & A. M. Lu	berry ovoid. Seeds few.	Calyx campanulate, ca.3×3 mm, usually (2-or) 3-divided to halfway, lobes sometimes with irregular teeth.	Branches innexed, with thoms 1–3 cm.
L. chinense Mill.	Dad avaid on ablance Coods avanceurs	Corolla tube cylindric, obviously longer than lobes, 5-6mm, ca. 2.5 mm in diam.; lobes broadly ovate, ca. 4 mm, margin pubescent.	Leaves solitary or in clusters of 2 or 3 on short shoots; leaf blade lanceolate, base cuneate, apex obtuse.
L. Chinense with.	Red, ovoid or oblong. Seeds numerous, yellow, 2.5–3 mm.	Pedicel 1–2 cm. Calyx campanulate, 3–4 mm, 3–5-divided to halfway, lobes densely ciliate. Corolla pale purple, 0.9-l.2 cm; tube funnel-form,	0.5–2 m tall. Stems much branched; branches pale gray, slender, curved or pendulous, with thorns 0.5–2 cm. Leaves solitaryor in clusters of 2–4; leaf blade
L. yunnanense	Globose, yellow-red when ripe, with an	shorter than or subequaling lobes, lobes pubescent at margin. Pedicel 4–6 mm.	ovate, rhombic, lanceolate, or linear-lanceolate. ca. 0.5 m tall. Branch lets yellow-brown, thorny at
Kuang & A.M. Lu	obvious longitudinal furrow on drying. Seeds ca. 20, pale yellow, orbicular, pitted.	Calyx campanulate, ca. 2 mm, usually 3-lobed or 3- or 4-dentate, tomentose at apex. Corolla pale blue-purple, purple, or occasionally	apex. Leaves solitary on long shoots, sometimes on thorns or fasciculate on tubercular short shoots; petiole short; leaf blade narrowly ovate to
	- 191	white, funnel form, 5–7 mm; tube 3–4 mm; lobes 2–3 mm, glabrescent.	lanceolate, base narrowly cuneate, apex acute.
L. europaeum L.	Reddish	Flowers solitary or in clusters of 2(-3). Calyx 2-3 mm, 5-dentate or 2-lipped. Corolla 11-13 mm, narrowly infundibuliform, pink or white; lobes 3-4 mm. Stamens usually exserted; filaments glabrous, somewhat unequal.	1–4 m tall; branches rigid, very spiny; spines stout. Leaves 20 – 50×3 – 10 mm, usually oblanceolate.
L. intricatum Boiss.	Orangc-red or black	Plant Flowers solitary or in c1usters of 2–3. Calyx 1.5–2 mm, shallowly 5-dentate. Corolla 13–18 mm, narrowly infundibuliform, blue-violet, purple, lilac, pink or white; lobes 2–3 mm. Stamens inc1uded; filaments glabrous.	0.3–2 m, much-branched, very spiny; spines stout, rigid. Leaves 3–15 \times 1–6 mm, oblanceolate.
L. afrum L.	Purplish	Calyx 5–7 mm, deeply 5-dentate. Corolla 20–22 mm, subcylindrical, purplish-brown; lobes ca. 2 mm. Stamens included; filaments with dense tuft of hairs	1–2 m; branches rigid, very spiny; spines stout. Leaves 10–23 \times 1–2 mm, very narrowly oblanceolate.
L. berlandieri Dunal	Red, globose to ovoid, glabrous.	at base. Solitary or in pairs, pedicels 3–20 mm long; calyx cup-shaped, 1–2 mm long, (3)4- or 5-1obed, the lobes usually shorter than the tube, glabrous except for a tuft of hair at the tip of each lobe; corolla blue, pale lavender, or ochroleucous, campanulate-funnelform, 6–7 mm long, the limb 4- or 5-1obed.	Erect shrub to 2.5 m tall, armed with needlelike spines on the younger shoots or nearly unarmed; branches somewhat crooked, glabrous. Leaves 1–3 in a fascicle, linear to elliptic-spatulate, glabrous, apex rounded to acute, margins entire, base attenuate to a short petiole or subsessile.
L. pallidum Miers	Red (drying blackish or purplish), glaucous, subglobose to ovoid, glabrous. Seeds yellowish, widely ovate to subreniform, minutely pitted.	Solitary or occasionally in pairs, pedicel 8–18 mm long; calyx campanulate, 5–9 mm long, 5-1obed, the lobes about equaling or slightly longer than the tube, glabrous; corolla greenish-white, sometimes tinged with purple, funnelform, 15–20 mm long, the limb 5-1obed.	Upright-spreading, much-branched shrubs to 20 dm tall, branches lightly pubescent to glabrous, sparingly armed with stout spines. Leaves mostly fascicled, except on young growth; blade oblanceolate or spatulate, 1–4 cm long, (3)5–15 mm wide, glabrous, apex acute to obtuse, margins entire, base attenuate; petiole 5–10 mm long. (continued on next page

Table 3 (continued)

Species	Berry	Flower	Stem and leaf
L. shawii Roem. & Schult.	Orange-red, 4 mm broad. Seeds ca. 1.5 mm broad, reniform, brown.	Solitary or paired, white or purple-suffused. Pedicel 3–4 mm long, pilose. Calyx narrow tubular, pilose; lobes 0.5–1 mm long, acute, pubescent. Corolla tube 10–12 mm long; lobes 2.0 mm long, acute, minutely pubescent. Filaments glabrous at the base, subexserted.	A spiny branched shrub 100–180 cm tall, shoots white-tomentose. Spines tomentose towards the base. Leaves 4–25 $(-30) \times 2.5$ –6 mm, ellipticoblong to narrow oblong, cuneate, obtuse or acute, pilose to tomentose.

Flora of China Editorial Committee (1994), Tutin (1972), McGregor and Barkley (1986) and Ali (1980).

Levin et al., 2011; GBIF, 2017). It was first published by Linnaeus, and three species (viz. *L. europaeum, L. barbarum*, and *L. afrum*) were described in Species Plantarum (Linnaeus, 1753). In 1932, Hitchcock published a systematic taxonomic study on 43 *Lycium* species from the western hemisphere based on morphology (Hitchcock, 1932). Recently, molecular markers of different genome parts were used to elaborate the phylogenetic relationship within the genus as well as biogeographic events: *Lycium* originated from the Americas, and then dispersed to Africa and Eurasia; the diversity centers are the Americas and Africa (Olmstead et al., 1999; Fukuda, 2001; Miller, 2002; Yin et al., 2005; Levin and Miller, 2005; Levin et al., 2009a, 2009b; Miller, 2011; Levin et al., 2011).

According to our findings, at present ninety seven species and six varieties are recognized (Table 2). Among them, 32 are native to South America, 24 to North America, 24 to Africa, and 12 to Eurasia; two occur in Eurasia as well as Africa. Lycium australe is the only species endemic to Australia, and L. sandwicense is native to the Pacific islands. L. carolinianum occurs in North America as well as the Pacific islands.

Lycium species are shrubs or small trees, often with thorns on the stem and simple, entire leaves. Usually they are differentiated through the thorn on the stem, the shape and size of leaves, the corolla length, the length of stamen, colour of the fruit, the taste of the fruits, and the size and number of seeds. Morphological characters of the typical frequently used species of different continents are summarized in Table 3. However, the commercial Lycium products are always without these characteristic traits as they are only few parts of the plant, e.g., fruit, root bark and leaf, therefore, morphological techniques solely were not sufficient for the authentication of Lycium products. For example, fruits of L. barbarum and L. chinense, the two most commonly used goji, are difficult to distinguish by eye (Xin et al., 2013), which is a challenge for quality assessment in trading.

3.2. Traditional uses

3.2.1. Traditional uses worldwide

Of all 97 species, 35 species and 2 varieties were found to be used as food and/or medicine (Table 2). The number of native species of the different continents used as food and medicine are shown in Fig. 1.

Although the richness of *Lycium* species differs in South America, North America, Africa and Eurasia, the numbers of species used are similar. Therefore, the species use ratios are dramatically different. In Eurasia, nine (64%) of the 14 species, and one variety, are used. While 86% of the *Lycium* species occur in the Americas and Africa, only 31% (26 species) of them are used as food and/or medicine. The Australian species as well as the two Pacific Island species are all used as food.

Of 28 species the plant parts used are the fruits, both for food and medicine, indicating that the fruit is worldwide the most commonly used plant part; of the other species also the leaves and root bark are used, and in some cases the whole plant. Leaves and root bark are usually used as medicine, while young shoots may also be prepared as food. Lycium barbarum, L. chinense, and L. ruthenicum are the most often reported species in the literature for China, L. europeaum, L. intricatum, and L. shawii for the Mediterranean and Middle East, L. pallidum for North America, and L. afrum for Africa. Usually the fresh or dried fruits are consumed, and the fresh leaves are cooked as food or used as tea. Of them, L. barbarum and L. chinense have been introduced as "superfood"

from China to Europe, the Americas, and Australia. They are typically consumed as food supplement.

3.2.2. Use of Lycium in China over time

Today, the dried fruits and the root bark of *L. chinense* and *L. bar-barum*, called *Gouqi Zi* and *Digu Pi*, are commonly used in Chinese medicine and diet (Wagner et al., 2011; Chang and So, 2015; Tan et al., 2017). Whether the same or different species have been used in the past is not easy to deduce from the historical herbals, as the species concept did not exist in earlier times; and in the older herbals, even the plant parts used were not recorded. Therefore, information has to be inferred from the Chinese characters and the plant figures in the historical herbals.

The Chinese characters "枸杞" (gǒu qǐ) means Lycium, although sometimes the word means the fruit of Lycium only. However, in the ancient literature the character "杞" alone was often referring to Lycium. "杞" was also present in the oracle bone script, a script which was used in Shang Dynasty (B.C.E. 1400 s to B.C.E. 1100 s), indicating that the use of Lycium has a long history in China. It also appeared in later scripts, like bronze inscription and seal script. The earliest record of using Lycium in China was found in the Book of Songs (诗经, shī jīng), which consisted of poems written in the Zhou Dynasty (B.C.E. 1100 s to B.C.E. 300 s) (Gao, 1980). In the 74 poems of the chapter Xiaoya (小雅, xiǎo yǎ), "杞" was mentioned six times. The sentences, "南山有杞 (nán shān yǒu qì" and "言采其杞 (yán cǎi qí qì", describe people harvesting Lycium plants growing in the mountains.

Records of *Lycium* in the Chinese herbals over time are listed in S1, while Fig. 2 shows *Lycium* illustrations. The earliest record of *Lycium* as medicine was in *Shennong's* Herbal (ca. C.E. 100) (Shang, 2008). The original herbal does not exist anymore, and the present edition was compiled from later citations. The text mentions the flavour, effects, common names, and habitat of *Lycium* briefly, but not the plant parts used (Li, 1954). Deduced from the given flavour, it might be the root; from the effects, it could be both fruits and roots; from the recorded common name "枸杞", it might be both fruits and roots, as some later herbals also used the same name for root and/or fruit.

In the *Jin* Dynasty (C.E. 266 – 420), *Ge Hong* (284 – 364) published two herbals, *Baopuzi* (Ge, 1995) and *Zhouhou Beiji Fang* (Ge, 1999), both of which included *Lycium*. The later was the first herbal with formulas, and *Lycium* fruit, root, and juice were recorded separately in different formulas. *Leigong Paozhi Lun* (ca. 420 – 479) (Lei, 1985), the first monograph on processing of *materia medica*, recorded the manufacture of the root bark, while the fruit decoction was used for processing another drug. *Mingyi Bielu* (Tao, 1986), published around C.E. 500, is commonly regarded as the first herbal describing the use of *Lycium* fruits; however, according to our research, *Lycium* fruits and root had already been used separately in earlier times (*Jin* Dynasty by *Ge Hong*).

Lycium was first recorded as food in Bencaojing Jizhu (ca. C.E. 500) (Tao, 1994). In Xinxiu Bencao (659) (Su, 1981) and Shiliao Bencao (ca. 700) (Meng, 1984), Lycium was also recorded as food, with several medicated diet recipes of the fruits, root, and leaves. Later, in Qianjin Yifang (682) (Sun, 1998), cultivation techniques of Lycium were described, beside its medicinal usages.

New in the Song Dynasty (960 - 1279) was the detailed morphological description of the plant accompanied by illustrations. Bencao

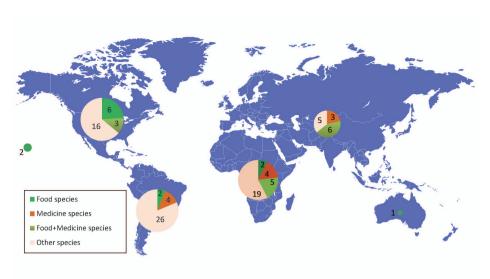


Fig. 1. *Lycium* species used as food and/or medicine on the different continents.

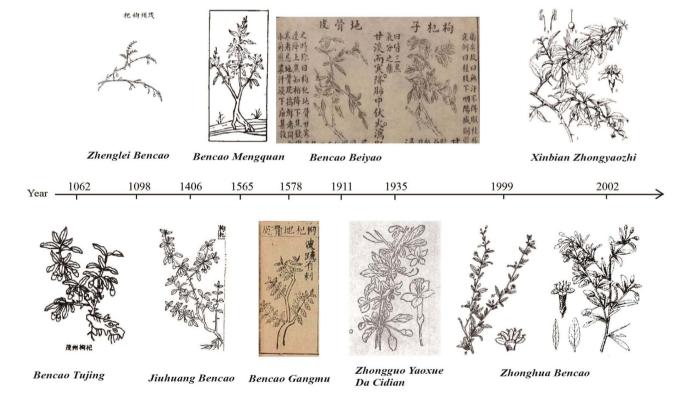


Fig. 2. Illustrations of Lycium in Chinese herbals over time.

Tujing (Su, 1994) and Zhenglei Bencao (Tang, 1982) were the most important herbals during Song, and Lycium was recorded in both.

In the *Yuan* Dynasty (1271 - 1368), the recipes of tea, porridge, and wine using the fruit or the leaves were recorded in the medicated diet monograph *Yinshan Zhengyao* (Hu, 2009).

Bencao Gangmu (1596) (Li, 1954), also known as Compendium of Materia Medica, discussed the habitat, the use history, manufacturing, and usage of Lycium, offering a review of former information as well as Li Shizhen's (1518 — 1593) understanding of its use. In the Ming and Qing Dynasty (1644 — 1912), many formulas containing Lycium emerged and were described in various herbals. In 1935, the herbal Zhongguo Yaoxue Da Cidian (Chen, 1935), for the first time published the scientific name Berberis lycium for 枸杞. This was later found to be a misidentification, and was replaced by Lycium. Besides the key herbals described above, there were still many interesting ones published in

different times (Chen, 1985, 1988, 2008; Du, 1975; Jiang, 1911; Kou, 1990; Liu, 1956; Lu, 1986; Ni, 2005; Wang, 1987; Wu, 1959, 1987; Yan, 1958; Yang, 1958; Zhu, 2008); as a result, these herbals conserved the food and medicine use history of *Lycium* in China.

The contemporary herbals, such as *Zhonghua Bencao* (Zhonghua Bencao Editorial Board, 1999), *Xinbian Zhongyao Zhi* (Xiao, 2002), and *Zhongyao Da Cidian* (Nanjing TCM University, 2006), refer to both L. *chinense* and L. *barbarum*. Precise botanical descriptions are provided and usages are combined with scientific findings and pharmacological evidence and guidance for use.

3.2.3. Traditional uses by Chinese ethnic minorities

In China, seven species and two varieties of the genus *Lycium* occur, of which four species have been used by different ethnic groups. We found use records for twelve of the officially recognized 55 ethnic

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Ethnic group	Distribution provinces	Species	Used parts	Indications and usages	References
藏族Tibetan	Tibet, Sichuan, Yunnan, Qinghai, Gansu	L. barbarum	Fruit, root, bark, leaf	Fruit, root, bark, leaf Cough, xiaoke (similar to diabetes), dizziness, fever, gynecopathy, night sweat, lumbar genu Jia and Li (2005); Yu (1996) aching and limp, leukorrhea, headache, amnesia, agrypnia, tuberculosis, spermatorrhea	Jia and Li (2005); Yu (1996)
		L. chinense	Fruit	Deficiency of the kidney and liver, anemia, cough, xiaoke, headache, heart hot, amnesia, agreements annessed to the second section of the second seco	Zhonghua Bencao Editorial Board
		L. dasystemum	Fruit	agstypus, gynecopaury Heart hot, gynecopathy	Jia and Li (2005)
:		L. ruthenicum	Fruit	Heart diseases, gynecopathy	Dimaer (1986); Jia and Li (2005)
维吾尔族Uighur Xinjiang	Xinjiang	L. barbarum/ L. chinense	Fruit	Hyposexuality, blurry vision, neurasthenia, hyperlipidemia, oligospermia	Editorial Board (2005a)
蒙古族 Mongol	Inner Mongol, Heilongjiang, Jilin, Liaoning, Xinjiang, Hebei, Qinghai	L. barbarum	Fruit	Xiaoke, giddy dazzled, tinnitus, lumbar genu aching and limp, deficiency of the kidney and liver, fever, stasis, amenorrhea, blurry vision	Jia and Li (2005); Zhonghua Bencao Editorial Board (2004)
苗族Miao	'unnan,	L. chinense	Root bark, fruit, leaf, whole plant	Fever, night sweat, dysphoric, cough and asthma, xiaoke, bleeding, eumatism, dizziness, swell, tuberculosis, blurry vision, deficiency of the kidney and liver, backache, fatigue, finger inflammation; medicated diet included	Editorial Board (2005b); Jia and Li (2005)
畲族She	Fujian, Zhejiang	L. chinense	Fruit, root, leaf, root bark	Sore throat, blurry vision, kidney deficiency and backache, male infertility, <i>xiaoke,</i> palpitation, insomnia, tears; medicated diet included	Song and Xu (2002); Jia and Li (2005)
土家族Tujia	Hubei, Hunan, Chongqing, Guizhou	L. chinense	Fruit, root bark	Blurred vision, giddy dazzled, spermatorrhea	Zhu et al. (2006)
景颇族Jingpo	Yunnan	L. barbarum	Fruit	Blurry vision, kidney deficiency, blood deficiency, neurasthenia	Jia and Li (2005)
德昂族De'ang	Yunnan	L. barbarum	Fruit	Blurry vision, kidney deficiency, blood deficiency, neurasthenia	Jia and Li (2005)
彝族Yi	Yunnan, Guizhou, Sichuan, Guangxi	L. chinense	Whole plant	Pruritus, sore and ulcer diseases	Jia and Li (2005)
朝鲜族Korean	Heilongjiang, Jilin, Liaoning	L. chinense	Fruit	Blurry vision, kidney deficiency, backache, neurasthenia, vomiting blood	Jia and Li (2005)
瑶族Yao	Guangxi, Hunan, Yunan, Guangdong	L. chinense	Root bark	Fever, night sweat, xiaoke, hyperlipidemia, tuberculosis	Liu (2002)
们族Dong	Guizhou, Hunan, Guangxi, Hubei	L. chmense	Fruit	Gum erosion and blooding	Jia and Li (2005)

minorities of China (Table 4).

Four species have been used in Tibetan medicine, while both *L. barbarum* and *L. chinense* by the Uighurs and either of them by the other ethnic groups. Fruits as well as root bark and leaves have been commonly used. The whole plant has been used by the *Miao* and *Yi* for different purposes: *Miao* use it as a tonic, while *Yi* use it for sores and itching. The *Miao's* usages are similar to the ancient Chinese herbals' records.

In general, *Lycium* spp. have often been used for the treatments of blurry vision, fever, night sweat, kidney deficiency, cough and asthma, diabetes, heart diseases, gynecopathy, and neurasthenia. However, the *Yi* and *Dong* use them differently, i.e. the fruits of L. *chinense* are for bleeding gums, while the whole plant as antipruritic drug. They were also used as medicinal food by the *Miao* and *Yi*.

3.2.4. Comparison of traditional uses with recent pharmacological studies

Different Lycium species, foremost L. barbarum and L. chinense, were phytochemically analyzed and hundreds of compounds were isolated and identified (Qian et al., 2017). Bioactivities and pharmacological effects of crude extracts or compounds were assessed in pharmacological studies and it turns out that many of the traditional uses are supported by these studies. For example, the anti-aging effect of Lycium (probably the whole plant of L. chinense or L. barbarum) has been recorded since Shennong's Herbal (ca. C.E. 100); recent studies demonstrated that polysaccharides, vitamins, pigments, and crude extracts of Lycium fruits are benefitting age-related lesions (Bucheli et al., 2011; Li et al., 2007; Kim et al., 1997; Tao et al., 2008; Yi et al., 2013). Use for improving eyesight was mentioned in herbals as well, and Zeaxanthin, lutein, and polysaccharides were found to have retinal protection activities (Tang et al., 2011; Mi et al., 2012b; Song et al., 2012; Chu et al., 2013; Pavan et al., 2014). Xiaoke is a term used in ancient herbals, describing symptoms similar to present diabetes (Li et al., 2004); Studies on root bark and fruits of L. chinense and L. barbarum found that water extract, polysaccharides, organic acids, and alkaloids have an effect on lipid metabolism and oxidative restoring of diabetic animals (Ye et al., 2008; Li, 2007; Luo et al., 2004). Also, an anti-fatigue and hepatoprotective effect of Lycium fruits and root bark has been shown recently (Alharbi et al., 2017; Xiao et al., 2012; He et al., 2012; Cui et al., 2012), and has been recorded in herbals too.

Since *L. barbarum* and *L. chinense* are widely used species, most phytochemical and pharmacological studies have been focusing on the fruits and root bark of these two species. As a result, there are scientific evidences for their medical use, which in turn have been increasing again their popularity. Therefore, they have been adopted in pharmacopoeias of many countries and regions. For example, in the current Chinese pharmacopoeia (2015), there are 75 prescriptions containing fruits of *L. barbarum*. They were also allowed to be used as cosmetic materials in China. In contrast, only a few studies focused on other *Lycium* species, which are less widely used (Table 5).

3.3. Lycium in current pharmacopoeias

3.3.1. Lycium in recent pharmacopoeias of the world

As sources of common herbal medicines, *Lycium* species have been incorporated into several pharmacopoeias, including China, Europe, Japan, Korea, Taiwan, UK, and Vietnam (Table 6). *Lycium* has not been included in the pharmacopoeia of USA, Russia, Africa, Australia, Brazil, Argentina, Switzerland, Iran, and India.

The fruit and/or root bark of *L. barbarum* and/or *L. chinense* are the most frequently used materials mentioned in the pharmacopoeias, although the aerial part of *L. barbarum* and *L. europeaum* are recorded by the Indian Ayurveda pharmacopoeia. The European pharmacopoeia only includes the dried fruit of *L. barbarum*.

Lycium fruits (Lycii Fructus) and Lycium root bark (Lycii Radices Cortex) are used in several regions officially, however, the quality criteria differ. Firstly, the species used as Lycii Fructus differ. Lycium

 Table 5

 General bioactivities of compounds or extracts of Lycium spp.

Bioactivity	Compounds, extracts, or plant materials	References
Antioxidant	Flavonoids, polysaccharides, pigments, mixed extracts,	Le et al. (2007); Li and Zhou (2007); Li et al. (2007); Bai et al. (2008); Donno et al. (2015);
	fatty acid	Benchennouf et al. (2017); Wang et al. (2010); Chung et al. (2014)
Spermatogenesis	Polysaccharides (fruit of <i>L. barbarum</i>)	Luo et al. (2014); Qian and Yu (2016); Shi et al. (2017)
Retinal protection	Zeaxanthin and/or lutein, polysaccharides	Tang et al. (2011); Mi et al. (2012b); Song et al. (2012); Chu et al. (2013); Pavan et al. (2014)
Hepatoprotective	Zeaxanthin dipalmitate, polysaccharides, betaine,	Alharbi et al. (2017); Xiao et al. (2012); Xiao et al. (2014b); Xiao et al. (2014a); Zhang et al.
	flavonoids, fruit	(2010); Ahn et al. (2014); Ha et al. (2005)
Anti-aging	Fruit, polysaccharides, vitamins, pigments	Bucheli et al. (2011); Li et al. (2007); Kim et al. (1997); Tao et al. (2008); Yi et al. (2013)
Immunomodulation	Polysaccharides-protein complex, polysaccharides,	Zhang et al. (2014); Tang et al. (2012); Chen et al. (2012); Chen et al. (2008); Chen et al.
	pigments	(2009a), (2009b); Xie et al. (2016); Gan et al. (2004)
Anti-tumor	Polysaccharides-protein complex, polysaccharides, mix	He et al. (2012); Cui et al. (2012); Tang et al. (2012); Hu et al. (1994); Gan et al. (2004); Liu
	extract, scopoletin and AA – 2βG	et al. (2000)
Skin care	Polysaccharides, juice, glycoconjugate	Reeve, et al., 2010; Liang and Zhang (2007); Zhao et al. (2005)
Anti-microbial	Lyciumoside I, AcOEt-soluble fraction	Terauchi et al. (1998); Lee et al. (2005); Kim et al. (2000)
Anti-diabetic	Water extract, polysaccharides, organic acids, and	Ye et al. (2008); Song et al. (2012); Li et al. (2004); Li (2007); Jia et al. (2003); Luo et al.
	alkaloids	(2004)
Anti-atherosclerosis	Seed oil, polysaccharides	Jiang et al. (2007); Ma et al. (2009)
Hypotensive	Water extract, polysaccharides	Kim et al. (1997); Mi et al. (2012a); Mi et al. (2012b)
Neuroprotective	Water extract, polysaccharides, alkaline extract	Ho et al. (2007); Chan et al. (2007); Ho et al. (2010); Mi et al. (2013); Wang et al. (2014)
Anti- fatigue	Polysaccharides, betaine	Wu and Guo (2015); Kim and Baek (2014)
Neuroprotective	Water extract, polysaccharides Water extract, polysaccharides, alkaline extract	Ho et al. (2007); Chan et al. (2007); Ho et al. (2010); Mi et al. (2013); Wang et al. (2013)

 $\begin{tabular}{ll} \textbf{Table 6} \\ \textit{Lycium} \ \mbox{records in current pharmacopoeias of the world.} \\ \end{tabular}$

Region	Pharmacopoeia	Species	Used parts	Description	Identification	Examination
China	Chinese Pharmacopoeia (Pharmacopoeia Commission, 2015)	L. barbarum	Fruit	Harvest, process, air dry, odour, taste, macroscopic, storage, indication	Microscopic, TLC	Loss on drying $\leq 13.0\%$, total ash $\leq 5.0\%$, water extract content $\geq 55\%$, polysaccharides $\geq 1.8\%$, betaine $\geq 0.30\%$ heavy metals
		L. barbarum/ L. chinense	Root bark	Yinpian; harvest, process, odour, taste, macroscopic, storage, indication	Microscopic, TLC	Loss on drying $\leq 11\%$, total ash $\leq 11\%$, acid-insoluble asl $\leq 3\%$
EU	European Pharmacopoeia (9.0) (2016)	L. barbarum	Fruit	Dried, whole, ripe fruit	Macroscopic, microscopic, TLC	Loss on drying \leq 13%, total ash \leq 5%, extract content \geq 55%
UK	British Pharmacopoeia Commision (2017)	L. barbarum	Fruit	Dried, whole, ripe fruit	Macroscopic, microscopic, TLC	Loss on drying \leq 13%, total ash \leq 5%, extract content \geq 55%
Japan	Japanese Pharmacopoeia	L. barbarum/ L. chinense	Fruit	Morphologic, odour, taste, storage	TLC	Foreign matters $\leq 2\%$, total ash $\leq 8\%$, acid-insoluble ash $\leq 1\%$, extract content (dilute ethanol) $\geq 35\%$
	(17th)(2016)	L. barbarum/ L. chinense	Root bark	Morphologic, odour, microscopic, taste, storage	TLC	Heavy metals, arsenic, loss on drying $\leq 11.5\%$, total ash $\leq 20\%$, acid-insoluble ash $\leq 3\%$, extract content (dilute ethanol) $\geq 10\%$
Korea	Korean Pharmacopoeia	L. barbarum/ L. chinense	Fruit	Morphologic, odour, taste	TLC	Foreign matters \leq 3%, total ash \leq 6%, betaine \geq 0.5%.
(11th)(2014)	(11th)(2014)	L. barbarum/ L. chinense	Root bark	Morphologic, microscopic	Colour test, TLC	Loss on drying \leq 12%, foreign matters \leq 5%, total ash \leq 18%, acid-insoluble ash \leq 3%, extract content(dilute ethanol) \geq 8%
	Korean Pharmacopoeia (9th)	L. barbarum/ L. chinense	Fruit	Morphologic, odour, taste	Colour test	Foreign matters \leq 3%, total ash \leq 6%, betaine \geq 0.5%.
	(2007) (Korea Food and Drug Administration, 2007)	L. barbarum/ L. chinense	Root bark	Morphologic, microscopic	Colour test, TLC	Loss on drying \leq 12%, foreign matters \leq 5%, total ash \leq 18%, acid-insoluble ash \leq 3%, extract content(dilute ethanol) \geq 8%
Taiwan	Taiwan TCM Pharmacopoeia (2nd)(2013)	L. barbarum/ L. chinense	Fruit	Macroscopic, indication, microscopic, storage	TLC	Total ash \leq 11%, acid-insoluble ash \leq 2%, aflatoxin \leq 15.0 ppb, extract content (dilute ethanol \geq 35%, water \geq 40%)
		L. barbarum/ L. chinense	Root bark	Macroscopic, microscopic, storage, indication	TLC	Loss on drying $\leq 14\%$, total ash $\leq 15\%$, heavy metal ≤ 16 ppm, As ≤ 6 ppm, extract content (dilute ethanol $\geq 8\%$, water $\geq 10\%$)
Vietnam	Vietnam Pharmacopoeia (4th) (2007) (Ministry of Health, 2010)	L. barbarum	Fruit	Macroscopic, microscopic, process, storage, indication	TLC	Loss on drying \leq 11.0%, total ash \leq 5.0%, extract conten \geq 55%, foreign matters \leq 1%
		L. barbarum/ L. chinense	Root bark	Macroscopic, microscopic, process, storage, indication	Macroscopic, microscopic, TLC	Loss on drying \leq 11%, foreign matter \leq 2%, total ash \leq 11%
India	Ayurveda API (Vol. 6) (Department of Ayush New Delhi, 2008)	L. barbarum/ L. europeaum	Aerial part	Macroscopic, microscopic	TLC	Foreign matters \leq 2%, total ash \leq 15%, acid-insoluble as \leq 2%, extract content (dilute ethanol \geq 4.5%, water \geq 20%)

chinense is accepted by the pharmacopoeias of Japan, Korea, and Taiwan, but not included in the pharmacopoeias of China, Europe, UK, and Vietnam; while they are not morphologically distinguishable, practically, both of them are consumed widely. Secondly, the descriptions are different. Indications are only included in pharmacopoeias of China, Taiwan, and Vietnam; macroscopic and microscopic traits are included to different degrees. Thirdly, the identification techniques differ. Colour test as primary identification tool, which could be used for detecting some chemical groups, is only used by the Korean pharmacopoeia; TLC, which is much more specificity based on chemical fingerprint and sufficient for species differentiation, is used widely. However, it was not included in the Korean pharmacopoeia until 2012. Lastly, the quality examination indexes and their thresholds differ as well. While betaine, a bioactive compound in Lycii Fructus, is used as index in the pharmacopoeia of China and Korea only, contents of polysaccharides are exclusively mentioned in the Chinese one.

3.3.2. Lycium in Chinese pharmacopoeias

Since 1949, there have been 10 editions of the Chinese pharmacopoeia (Chinese Pharmacopoeia Commission, 1963, 1977, 1985, 1990, 1995, 2000, 2005, 2010, 2015). *Lycium* species described in the different editions are shown in Table 7.

Lycium was not included in the first edition of the Chinese pharmacopoeia which was published in 1953. While in 1963 L. barbarum and L. chinense were mentioned for their fruits and L. chinense for its root bark. This changes afterwards and L. barbarum was documented for its fruits while both, L. chinense and L. barbarum were used for their root barks.

The descriptions of *Lycii Fructus* and *Lycii Radices Cortex* of all editions were similar, but macroscopic traits became more and more detailed over time. Identification and examination indexes, however, changed greatly. In the 1963 edition, the identification was based on macroscopic traits only, later, microscopic, total ash, TLC, loss on drying, impurities, contents of extracts, acid-insoluble ash, and heavy metals were included in succession. The development of pharmacopoeial monographs indicates the progress of quality control of herbal medicines.

Besides the pharmacopoeia, there are still some regional medicinal criteria which are published by provinces of China. Since the environments and the customs may differ among provinces, the records are diverse. For example, in *Ningxia*, the pedicel of the fruit and leaves of *L. barbarum* are officially used; in *Xinjiang*, the fruit of *L. dasystemum* has been accepted; in *Gansu*, the root bark of *L. truncatum* has been an official source of *Lycii Radices Cortex* (Li, 2001).

Accordingly, in China the quality criteria of *Lycii Fructus* and *Lycii Radices Cortex* have experienced notable developments over time, and they vary by geographic regions.

3.3.3. Comparison of Lycium records among pharmacopoeias

As demonstrated above, the fruits and/or root bark were adopted by pharmacopoeias of many countries and regions, as well as Chinese pharmacopoeias of different times; however, the descriptions and quality requirements were different. In order to understand the relationship of these pharmacopoeias, we extracted the parameters which were used for the identification of *Lycium*. The Indian Ayurveda pharmacopoeia was not included as it describes the aerial parts of the plant as a medicine, and the Chinese pharmacopoeia 1953 was excluded since it does not record *Lycium*. The results are shown in Fig. 3.

By the parameters of fruit, pharmacopoeias are firstly categorized into two groups: those of Taiwan, Japan, and Korea are with the earlier editions of Chinese pharmacopoeia, while European pharmacopoeia 9.0 (shown as EU 2016), British Pharmacopoeia Commision (2017) (UK 2017, which is the same as EU 2016), and Vietnam pharmacopoeia IV (shown as VN 2007) are similar to the later editions of Chinese pharmacopoeias (2000–2015). The difference between KR 2007 and KR 2014 is that the later includes TLC as an identification technique, and

they have a lower similarity with others. Pharmacopoeia of Taiwan and Japan are closely related and are separated from the earlier Chinese editions. The clustering also shows the development of Chinese pharmacopoeias over time: the ones before 2000 are separated from the ones since 2000; the reason is probably that the later include more examination items such as moisture and total ash.

By the data of root bark, EU 2016 and UK 2017 are separated from others since it does not adopt root bark. Pharmacopoeias of Taiwan, Japan, and Korea are in the same branch excluded from the Chinese ones. Like the result from the fruit, pharmacopoeias of Taiwan and Japan are again in the same group; VN 2007 is similar to the later Chinese ones since 2000 (except for the 2005 edition). If we consider the Chinese ones, the development is also presented by the clustering. However, the one of 2005 is grouped with the earlier ones; this may be because TLC was omitted.

Accordingly, the clustering is a practical tool to study the development of pharmacopoeia over time, as well as to reveal the relationship among pharmacopoeias of different regions.

4. Discussion

According to our study, 35 out of 97 Lycium species worldwide have been recorded to be used as food and / or medicine. The species use ratio in the Americas is rather low, maybe because there are many species available there. Alternatively, it would be worth to investigate the abundance of different species in the relevant regions in order to better understand the potential access to these resources. The thorny Lycium species are generally ignored. In order to make better use of lessused Lycium species, phytochemical and pharmacological studies are needed.

Only *L. barbarum* and *L. chinense* have been transformed into globally traded commodities and are marketed worldwide as a "super food". In China, based on the Chinese name "枸杞" their use can be traced back over the last two millennia. However, identification of the plant species and plant parts used is often not possible with certainty. Nevertheless, the use of *Lycium* fruits for anti-aging, improving eyesight and nourishing can be traced back at least C.E. 500 in *Mingyi Bielu*, and these usages still continue until today in Chinese medicine.

The diversity of plant usages offers opportunities for the development of new food and or medicine products. However, challenges for the quality control will have to be overcome. According to our study, different parts of *Lycium* species are used, and both of the botanical resources and traditional knowledge are primary materials for developing traditional herbal products (Jütte et al., 2017; Tu, 2015; Ngo et al., 2013). On the other hand, those differences set obstacles with regards to the quality control of the products, and the quality criteria differ greatly among regions. Along with the popularity of the fruits of *L. barbarum* and *L. chinense*, they become global consumables. However, almost all the goji are produced in China, and the exporters have to adjust their products to meet the diverse quality requirements of different regions; the different quality criteria among regions will probably obstruct the international trading. Therefore, a relative uniform quality criterion is recommended.

In general, recent pharmacological findings on *L. barbarum* and *L. chinense* largely support traditional uses as described in ancient herbals. Especially polysaccharides, zeaxanthin dipalmitate, vitamins, betaine, and mixed extracts were reported to be responsible for anti-aging, improving eyesight, anti-fatigue effects. It is obvious that detailed pharmacognostical studies lay a solid foundation for the wide acceptance of the plants and their products. Therefore, researches also need to focus on those less well-studied species but with interesting biological activities (Yao et al., 2011; Qian et al., 2017) as potential new sources of (healthy) foods or medicines. Due to the complexity of herbal preparations, quality control using only few chemical indicators is insufficient. Instead, the metabolomic approaches need to be developed (Donno et al., 2016).

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 Table 7

 Lycium records in Pharmacopoeias of China.

Year/ edition	species	Used part	Description	Identification	Examination
1953	NM	NM	NM	NM	NM
1963	L. barbarum/ L. chinense	Fruit	Harvest, process, odour, taste, indications, storage	Macroscopic	NM
	L. chinense	Root bark	Harvest, process, odour, taste, indications, storage	Macroscopic	NM
1977	L. barbarum	Fruit	Harvest, process, odour, taste, macroscopic, indications, storage	NM	NM
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, indications, storage	Microscopic	NM
1985	L. barbarum	Fruit	Harvest, process, odour, taste, macroscopic, indications, storage	NM	Foreign matter ≤ 1%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic	NM
1990	L. barbarum	Fruit	Harvest, process, odour, taste, macroscopic, indications, storage	NM	Foreign matter ≤ 1%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic	Total ash ≤ 11%
1995	L. barbarum	Fruit	Harvest, process, sun dry or air dry, odour, taste, macroscopic, indications, storage	NM	Foreign matter ≤ 2%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic	Total ash ≤ 11%
2000	L. barbarum	Fruit	Harvest, process, air dry, odour, taste, macroscopic, indications, storage	TLC	Loss on drying \leq 13.0%, total ash \leq 5.0%, foreign matters \leq 0.5%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Total ash ≤ 12%
2005	L. barbarum	Fruit	Harvest, process, air dry, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Loss on drying \leq 13.0%, total ash \leq 5.0%, water extract content \geq 55%, polysaccharides \geq 1.8%, betaine \geq 0.30%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic	Total ash ≤ 11%
2010	L. barbarum	Fruit	Harvest, process, air dry, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Loss on drying \leq 13.0%, total ash \leq 5.0%, water extract content \geq 55%, polysaccharides \geq 1.8%, betaine \geq 0.30%, heavy metals
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic, TLC	
2015	L. barbarum	Fruit	Harvest, process, air dry, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Loss on drying $\leq 13.0\%$, total ash $\leq 5.0\%$, water extract content $\geq 55\%$, polysaccharides $\geq 1.8\%$, betaine $\geq 0.30\%$, heavy metals
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indication, storage	Microscopic, TLC	Loss on drying \leq 11%, total ash \leq 11%, acid-insoluble ash \leq 3%

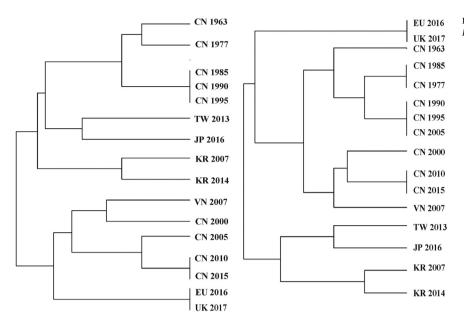


Fig. 3. Clustering based on parameters of Lycium fruit (left) and Lycium root bark (right) in different pharmacopoeias.

Historical documentary evidences are good basis for ethnobotanical study (Heinrich et al., 2006, 2012; Jütte et al., 2017). The historical continuity of Chinese medical herbals showcase the evolution of peoples' medical knowledge and offer ideas for treatment options for current diseases. In this study, the use history of Lycium in China was mapped out using the herbals, and some of the reported effects involved, such as anti-aging, retinal protection, and anti-fatigue, have been demonstrated experimentally. However, there are gaps between the descriptions in Chinese herbals and modern concepts: 1) the species are often not properly described as most of them were not written by botanists but doctors; 2) the terms of diseases and the description of symptoms are difficult to understand because of the difference of medical concepts; 3) the herbals contain historical "clinical data" and both the right and inaccurate information are included. As a result, the herbals are important sources of medicinal and nutritional researches, but they need to be used dialectically.

5. Conclusions

A comprehensive understanding of a species' characteristics, which includes taxonomy, geographic distribution, traditional use, phytochemistry, pharmacology, knowledge evolution, and quality control, is indispensable for finding new sources for food and/or medicine. This article highlights the need for a very sound understanding of the multicontextual basis of what is commonly termed a species 'traditional use'. The research approach used had to be transdisciplinary and the integration of historical, modern ethnobotanical, botanical, phytochemical and pharmacological data has enabled a much more detailed understanding of the genus as a whole and its wider potential. It also highlights that the focus so far has only been on two species and that the genus can potentially yield a wide range of other products with different properties.

This research has relied heavily on historical documentary evidences and such sources are good starting points for ethnopharmacological studies. In the present work, a set of time-continuous historical herbals of Chinese medicine generated a database on its usage and has allowed us to better understand the evolution of knowledge about *Lycium*. Hopefully, this ethnobotanical review incorporating both space and time dimensions will serve as a model for studying traditional food or medicine plants.

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Author contributions

All authors developed the concept for the study; R. Yao conducted the literature survey and drafted the paper. C.S. Weckerle and M. Heinrich supervised the work, and revised the manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jep.2017.10.010.

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