The introduction of an invasive weed was not followed by the introduction of ethnobotanical knowledge: A review on the ethnobotany of *Centaurea solstitialis* L. (Asteraceae)

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Invasive plants are known for their impacts to ecosystems and societies, but their potential cultural use tend to be unexplored. One important mechanism of plant invasion is the use of "allelochemicals" or "novel weapons": chemical defenses which are new to their invaded habitats and that confer them competitive advantages. However, these chemicals are precisely what confers them ethnobotanical and medicinal properties. Invasive species provide real time insights into the cultural processes by which humans learn to use plants. We aimed to assess the extent to which the introduction of a weed native to Eurasia into several non-native world regions was paralleled by the spread of cultural uses from its native range. We reviewed the literature assessing the biogeography of the cultural uses of the model invasive plant yellow-starthistle (*Centaurea solstitialis* L.; Asteraceae). We found that the species was rich in pharmaceutically active compounds and that the species had been traditionally used for medicinal purposes, as raw material, and as food. However, ethnobotanical uses were reported almost exclusively in its native range, with no uses described for the non-native range, apart from honey production in California, Argentina, and Australia. Our study exemplifies how, when plant introductions are not paralleled by significant human migrations, cultural adoption can be extremely slow, even within the native range of the species. This study highlights how biological invasions and cultural expansions can be subjected to different constraints.

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Abstract

19   Invasive plants are known for their impacts to ecosystems and societies, but their potential

20   cultural use tend to be unexplored. One important mechanism of plant invasion is the use of

21   "allelochemicals" or "novel weapons": chemical defenses which are new to their invaded

22   habitats and that confer them competitive advantages. However, these chemicals are precisely

23   what confers them ethnobotanical and medicinal properties. Invasive species provide real time

24   insights into the cultural processes by which humans learn to use plants. We aimed to assess the

25   extent to which the introduction of a weed native to Eurasia into several non-native world

26   regions was paralleled by the spread of cultural uses from its native range. We reviewed the

27   literature assessing the biogeography of the cultural uses of the model invasive plant yellow-

28   starthistle (*Centaurea solstitialis* L.; Asteraceae). We found that the species was rich in

29   pharmaceutically active compounds and that the species had been traditionally used for

30   medicinal purposes, as raw material, and as food. However, ethnobotanical uses were reported

31   almost exclusively in its native range, with no uses described for the non-native range, apart

32   from honey production in California, Argentina, and Australia. Our study exemplifies how, when

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35   invasions and cultural expansions can be subjected to different constraints.

Introduction

39   Invasive weeds can break havoc in the non-native regions that they invade, but in their native

40   range they are usually considered an inconvenient but not highly problematic native weed

41   (Hierro, Maron & Callaway, 2005; Montesinos, 2021). The reasons are multiple, including the

42   presence of other plant competitors, herbivores, pathogens, and parasites that share a long

43   evolutionary history with the weed (Callaway & Maron, 2006; Enders et al., 2020). An important

44   factor involved in the disproportionate success of invasive plants can be the use of "novel

45   weapons" (Callaway et al., 2008). This term refers to the presence of plant chemical defenses

46   that are new to the invaded plant communities, giving invasives a disproportionate success in

47   their non-native ranges (Hierro & Callaway, 2003). However, in their native range, natural

48   communities have been exposed to these chemicals for extended periods of time in what can be

49   considered as an evolutionary arms race, conferring native communities a tolerance to these

50   chemicals (Schaffner et al., 2011). These plant chemical compounds are precisely the ones

51   responsible for the numerous ethnobotanical and medicinal uses that can frequently be found at

52   the native ranges of these weeds. Interestingly, an study of medicinal uses of alien plants

53   introduced into South America found that alien weeds can become an important component of

54   the local pharmacopeias (Bennett & Prance, 2000) and another study found that in the Mexican

55   region of Chiapas the proportion of alien weeds used for medicinal purposes was higher than

56   should be expected given their relative abundance (Stepp & Moerman, 2001).

57   With the intensification of globalization and trade, humans have intentionally or accidentally

58   lead to the spread of alien invasive plants from one environment to another, and plants that were

59   considered economically and ecologically valuable in their native regions became unwanted

60   invaders in the introduced areas. Traditional use could be of great importance to understand the

61   idiosyncrasy of invasive species from their very origins, and thus to develop new research and

62   management plans. However, very little attention is given to the traditional use accumulated

63   through the centuries in the native ranges of these species, and we have very scarce information

64   on the extent to which at least part of this cultural knowledge spreads together with a biological

65   invasion. Compiling and synthesizing the ethnobotanical use available for invasive plant species

66   may help to identify pharmaceutical research targets, particularly if the invasive plant could

67   substitute overexploited native medicinal species. This may also proof useful for the

68   development of strategies to control invasive species. Although highly controversial, some

69   authors claim that one of the best strategies to control invasive species is through consumption

70   (see review in (Nuñez et al., 2012). For instance, in the native range of the weed *Centaurea*

71   *solstitialis* L. the plant is traditionally fed to sheep (Kargioğlu et al., 2008), and it has been

72   proven that livestock grazing is an effective way to reduce the number of *C. solstitialis* flower

73   heads with about 75% to 90% in the invaded region of California, where grazing has been used

74   as a measure of biological control (Thomsen et al., 1993).

75   In this study we reviewed the ethnobotanical literature available for a model invasive plant

76   species, *C. solstitialis* L. (Asteraceae), native from Eurasia and invasive across the Americas and

77   Australia, and to compare it with any reference or reports of cultural and ethnobotanical use

78   across the world regions in which it is considered invasive. It is an annual forb adapted to

79   disturbed environments (Grime, 1974; Xiao et al., 2016). Seeds of the species were introduced as

80   a contaminant of agricultural seeds in many regions around the world over the last two centuries

81   (Wang et al., 1991; Eriksen et al., 2014; Irimia et al., 2021). Although it is considered a noxious

82   weed in most of its introduced range, in its native range this species has been subject to cultural

83   experimentation locally, becoming an important element in the local culture and gastronomy

84   (Guarrera & Lucia, 2007; Lentini & Venza, 2007; E. Farouji & Khodayari, 2016; Licata et al.,

85   2016; Geraci et al., 2018), traditional medicine (Güneş, 2017), or as raw material (Kargıoğlu et

86   al., 2010). Many studies have been carried out to identify the chemical compounds that make this

87   plant pharmacologically relevant, and so far it is known that the species possesses many

88   sesquiterpene lactones with a broad spectrum of biological activities (Özçelik et al., 2009), which

89   are variable across the world (Irimia et al. 2019). Additionally, *C. solstitialis* is regarded as an

90   important plant for honey production in California, (Zouhar, 2002).

91   This review aims to exemplify how the study of the ethnobotanical use of a model invasive

92   species can provide with important information about the biogeography and history of

93   ethnobotany, and also for weed management in the non-native range. We aim to summarize the

94   available information about traditional uses, pharmacological activities, phytochemistry, and

95   toxicological research available, to identify knowledge gaps, and to provide a scientific basis for

96   potential applications in resource management. Finally, we aim to shed light on whether, and to

97   what extent, ethnobotanical knowledge can be transmitted when a exotic species is introduced

98   across different world regions.

99

100   **Methodology**

101   *Model study species*

102   Yellow star-thistle (*Centaurea solstitialis* L.; Asteraceae) is an erect winter annual weed

103   (occasionally biennial), which usually grows up to 1 meter tall, sometimes up to 2 meters tall,

104   with spiny yellow-flowered heads (DiTomaso, 2001). Anatolia and the Caucasus are considered

105   to be the ancestral range of the species (Eriksen et al., 2014), from where it went through a step

106 wise range expansion into central and southern Europe which is nowadays regarded as

107 adventitious or "expanded range" (Hierro et al., 2009). Several subspecies of *C. solstitialis* have

108 been described throughout the native range, four in Europe (Garcia-Jacas et al., 2006) and three

109 in the Asian part of Turkey. Starting in the mid-1800s, *C. solstitialis* was introduced as an

110 agricultural seed contaminant in many regions around the world, including the western United

111 States (USA), southern South America, southern Africa, and southern Australia (non-native

112 range) (Hierro et al., 2016). The degree of invasive success is variable across the introduced

113 range, with the species being highly damaging in Argentina and California (USA) (Hierro et al.,

114 2011). *Centaurea solstitialis* is consistently diploid across its native and non-native ranges, and

115 thus invasive success is attributed to other life history and ecological traits (Irimia et al. 2017).

116 This plant is a major consumer of ground water and it costs the California state millions of

117 dollars in water loss for wildlife, agriculture, and municipal uses. It was estimated that in the

118 year 2004 the water lost from plants of *C. solstitialis* in the Sacramento River watershed costed

119 between $16 million and $75 million dollars per year (calculated using the June 1999 CALFED

120 cost estimates) (Gerlach, 2004). Total losses of livestock forage value due to *C. solstitialis*

121 infestations on private land for the state of California were estimated at $9.45 million per year

122 (Eagle et al., 2007). Although data on other invaded regions is scarce, it is expected that

123 economic impacts could also be significant.

124 *Data collection*

125 The available information on *C. solstitialis* was collected using Google Scholar and the Web of

126 Science during 2019, using the search term: <"*Centaurea solstitialis*" or "*C. solstitialis*" and

127 "ethnobotany" or "ethnobotanical" or "medicinal" or "chemistry" or "traditional uses">. Thirty-

128 one articles published between January 1978 to December 2018 pertaining to the chemistry,

129 ethnobotany, pharmacology and toxicology of *C. solstitialis* were identified and reviewed.

130 Although there is a possibility that some articles written in languages other than English may

131 have been omitted by our search engine, it unified several data sources in a comparable manner,

132 facilitating the access to unconnected studies to provide valuable emerging information as a

133 result. The information retrieved from the papers (country and region of origin of the plants,

134 common local name, category of use, parts of the plant used, specific uses, preparation, and the

135 name of the authors of the studies) was compiled into a table (Supplemental Table 1). Each line

136 corresponds to a category of use mentioned in an article (1 or 2 lines per article), as some articles

137 mention more than one type of use for this species. Information about the chemical volatile

138 compounds was also summarized in a table (Supplemental Table 2). A range of relative

139 abundance (%) was calculated based on the articles that made this information available. This

140 includes the relative abundances of the compound in all the regions where it has been found,

141 ranging from the lowest value to the highest value found for each compound. Two articles from

142 California (Beck, Smith & Merrill, 2008; Oster et al., 2015) were not considered in the "Range

143 (%)" row due to a lack of information about this variable. One article from Algeria (Lograda, T.,

144 Ramdani, M., Chalard, P., Figueredo, G., Khalfoune, K. Silini, 2013) was excluded in the "Parts

145 of the plant" row because this information was not available in the paper.

146

147 **Results**

148 ***Economic importance***

149 *Traditional uses in the native range*

150 Traditional uses of *C. solstitialis* were found almost exclusively in its native range. The plant is

151 used for many purposes, which have been grouped into three major categories: medicinal, edible,

152 and raw material. A total of 31 articles on the traditional uses of the species have been found in

153 different countries of the Mediterranean and Western Asia (see Figure 1).

154 Most of the reported uses are medicinal (Figure 2), and include the treatment of i) respiratory

155 ailments (common colds in humans and animals); ii) digestive ailments (dysentery, stomach and

156 abdominal pain); iii) viral infections (herpes); iv) protozoa diseases (malaria); v) lesions of the

157 soft tissues and skin (mouth sore in humans and animals, boils and warts, skin rash); vi) eye

158 conditions or vii) or urolithiasis (kidney stones). The plant is also used as antipyretic, stomach

159 tonic and diuretic. All aerial parts of the plant are used as food in Italy, Iran, Saudi Arabia and

160 Turkey, being included in soups, or fried with eggs, used in pastry or simply boiled (Guarrera,

161 1994; Lentini & Venza, 2007; Licata et al., 2016; Geraci et al.,2018; Al-Sodany et al.,2013;

162 Ertug, 2004; Akan et al., 2013; Kargıoğlu et al., 2008). Aerial parts are also dried and fed to

163 sheep during winter. Its stems and branches are used to make brooms in Turkey (Kargıoğlu et al.,

164 2010) (Supplemental Table 1, Figure 2).

165 *Honey production*

166 The value of *C. solstitialis* for honey production is well known in its native range, and it is listed

167 as a plant species that produces unifloral honey in Europe (Persano Oddo et al., 2004).

168 Interestingly, the extensive monocultures that the species forms has resulted in a significant use

169 for honey production in the introduced ranges. This phenomenon has been well documented in

170 California (Zouhar, 2002). It was calculated that 150 000 colonies of bees in California depended

171 upon yellow starthistle for their primary source of pollen back in 1954 (Cordy, 1954), and in

172 1985 it was estimated to yield US$150 000 to US$200 000 per year (Maddox, Mayfield &

173 Poritz, 1985). Although it is an economically important plant, it is believed that the movement of

174 honeybee colonies by beekeepers may inadvertently assist the further spread of this plant in the

175   North-American range, because the species is predominantly an outcrosser species and it relies

176   on pollinators (mainly honey bees) to set seeds. In Argentina it has been observed that honey

177   bees visit this species intensively for pollen collection, and that the honey made of *C. solstitialis*

178   pollen contained a high level of protein (Andrada & Telleria, 2005). (Naab, Tamame &

179   Caccavari, 2008) characterized the honey of *C. solstitialis* produced in Argentina as being white,

180   with low pollen loads and with a pH varying from 3.19 to 4.06. There is also pollen from this

181   species in the honey produced in south Australia (Somerville, 2005), and it has been rated 5 in a

182   scale of 1-5 by (Birtchnell, M. J., Gibson, 2008) for possessing a "very high quality" for honey

183   production.

184   ***Phytochemical constituents and secondary metabolites***

185   The interest of the scientific community in the chemistry of *C. solstitialis* began when it was

186   proven to be causing a neurotoxic disease in horses in California. Many authors have been trying

187   to identify and characterize the chemical profile of the species since 1954. (Cassady &

188   Hokanson, 1978) were the first to identify the triterpene 3α, 16α-Dihydroxytaraxene-3-acetate.

189   Several sesquiterpene lactones (repin, subluteolide, acroptilin, janerin and cynaropicrin) were

190   identified in *C. solstitialis* by (Merrill & Stevens, 1985). (Jakupovic et al., 1986) identified a

191   guaianolide and a germacranolide (sesquiterpene lactones) and two bisabolone derivatives for the

192   first time. (Masso, J. L., Bertran, M. N., Adzet, 1979) found phenolic compounds, flavonoids,

193   tannins and terpenoid and phytosterol derivatives in *C. solstitialis*. (Thiessen & Hope, 1969)

194   isolated the sesquiterpenic lactone solstitialin and revealed its structure and configuration for the

195   first time.

196   The analysis of the essential oil of *C. solstitialis* carried out up to date through gas

197   chromatography - mass spectrometry (GC/MS) has provided a complete list of volatile chemical

198   compounds and their relative abundance. (Buttery et al., 1986) found out that germacrene D was

199   the major volatile constituent of the flower buds of *C. solstitialis* plants collected in California.

200   Other studies carried out in California also found germacrene D in higher concentrations than

201   other compounds (Beck, Smith & Merrill, 2008; Oster et al., 2015). (Binder, Turner & Flath,

202   1990) analyzed the constituents of three different parts of plants collected in Turkey and

203   identified 62 compounds including 22 sesquiterpenes, 11 C13 polyacetylenes, 10 aldehydes, 7

204   acyclic and 1 cyclic olefinic hydrocarbon, 5 alcohols, 2 ketones, 1 acid and 1 ester. Germacrene

205   D was also the major compound in these plants. (Esmaeili et al., 2006) analysed the essential oil

206   of the aerial parts of *C. solstitialis* from Iran and it was composed of eight monoterpenes

207   (16.5%), nine sesquiterpenes (39.3%) and one aliphatic acid (30.8%). The major compounds

208   were hexadecanoic acid and caryophyllene oxide, followed by 1,8-cineole and caryophyllene.

209   (Senatore et al., 2008) analysed the volatile compounds of *C. solstitialis* ssp. *schouwii* from Italy

210   and the main compounds were caryophyllene and caryophyllene oxide. (Carev et al., 2017)

211   analysed the essential oil of the aerial parts of *C. solstitialis* from Croatia. The main compounds

212   were nonoxigenated sesquiterpenes (23.8%), with germacrene D the dominant one, followed by

213   longifolen (3.6%) and b-caryo-phyllene (1.6%). Aliphatic acids were the most abundant among

214   nonterpene components, representing 44.4% of the total oil. (Lograda, T., Ramdani, M., Chalard,

215   P., Figueredo, G., Khalfoune, K. Silini, 2013) found 41 compounds in plants collected in

216   Algeria, being the most represented n-heneicosane (17.30%), hexadecanoic acid (12.79%), n-

217   tricosane (10.51%), n-pentacosane (5.64%) and caryophyllene oxide (5.03%).

218   (Sotes et al., 2015) focused on the leaf surfaces, which represent the first line of plant defense

219   against herbivores and analyzed the epicuticular chemistry of plants originating from native and

220   non-native regions. A high amount of sesquiterpene lactones were found, but the epicuticular

221   chemistry showed variation among regions, suggesting that the plant changes its chemistry

222   according to the demanding of the environment. Three sesquiterpene lactones were identified for

223   the first time in *C. solstitialis*: epoxyrepdiolide derivative, solstitialin A-3 13 diacetate and

224   linichlorin A. In a more recent study, Irimia et. al. (2019) applied the same methodology as

225   (Sotes et al., 2015), but analyzed more regions to have a more complete overview of the inter-

226   regional variations. These authors also observed that the plants from the non-native range were

227   more allelopathic, inhibiting the germination of seeds of other species significantly more than

228   plants from the native range, which was consistent with the novel weapons hypothesis (Callaway

229   & Ridenour, 2004).

230   A total of seven articles revealing the chemical compounds of *C. solstitialis* and their relative

231   abundance (%) were found. Despite some differences in the methodology used to obtain the

232   plant extracts and to perform the chromatographic analysis, these data were put together and

233   compiled in a table to systematize all the chemical compounds that have ever been identified in

234   *C. solstitialis* plants around the globe (Supplemental Table 2). These studies have been carried

235   out using plants from the native range (Turkey, Croatia, Italy, Iran and Spain) and from the non-

236   native range (California, Argentina, Australia and Chile). Different parts of the plant have been

237   analyzed, including leaves, stems, flower heads, flower buds and aerial parts in general. To

238   obtain the oil most of the authors grinded the plant parts to identify all the compounds present in

239   the plants, while two authors (Sotes et al., 2015); Irimia et. al., 2019) analyzed only the leaf

240   surface chemicals without damaging the leaves. A total of 161 compounds have been recorded in

241   some part of the plant, with 108 only present in plants from the native range. Among these

242   compounds, 44 were found only in Turkey. Only 7 compounds were found exclusively in the

243   non-native range, 2 terpene compounds: cynaropicrin 3-acetate, cynaropicrin 4´-acetate; and 5

244   nonterpene compounds: (E)-β-ocimene, (Z)-3-hexeno, (Z)-3-hexenyl propionate, 2-

245   methoxytoluene, perillene. The fact that most unique compounds were found in Turkey (Figures

246   3 and 4) is supportive of this region as the center of speciation of the taxon, and suggests that this

247   region could possess the largest genetic and functional diversity for the species. This is in

248   agreement with the results obtained by (Eriksen et al., 2014), which revealed great heterogeneity

249   for gene diversity, allelic richness and private allele values among populations in Eurasia, with

250   plant populations from Turkey scoring the highest levels of genetic diversity.

251   The compounds which are present in higher concentrations (over 20% per sample) are repin,

252   reaching the highest abundance in Chile; subluteolide with higher abundance in Australia;

253   hexadecanoic acid and caryophyllene oxide, both reaching the higher concentrations in Iran.

254   These are followed by janerin, epoxyrepdiolide, α-Linolenic acid, n-heinecosane and germacrene

255   D (15%-20%). Six of these compounds are sesquiterpenes.

256   The most geographically transversal compound, found in 8 of the 9 countries, was heptacosane.

257   The terpene compounds found in a higher variety of countries were the pentacyclic triterpenoids

258   α-amyrin, β-amyrin and taraxasterol, and the sesquiterpene lactones solstitialin A-13 acetate,

259   acroptilin, epoxyrepdiolide, janerin, repin and subluteolide. Plants from the native range

260   (Algeria, Croatia, Italy, Turkey) tend to have higher amounts of nonterpene in relation to terpene

261   compounds. The opposite is observed in non-native ranges with California as the region with a

262   higher diversity of terpenes (Figure 5),

263   *Pharmacology*

264   *Antioxidant*

265   (Şen et al., 2013) found out that the methanolic extracts of capitula and aerial parts of the *C.*

266   *solstitialis* had good effects on scavenging free radicals despite having small amounts of

267   phenolic compounds. (Koc et al., 2015) went further and tested *C. solstitialis* for its potential

268   medicinal action of biological targets that are participating in the antioxidant defense system

269   such as catalase (CAT), glutathione S-transferase (GST), and glutathione peroxidase (GPx). The

270   results showed high GPx and GST enzyme inhibition activity with acetone extracts from the

271   flower of *C. solstitialis*, with IC50 (half maximal inhibitory concentration) values of 79 and

272   232 ng/mL, respectively.

273   *Antiulcerogenic*

274   *Centaurea solstitialis* has been used in the Turkish culture for many years to treat ulcers and

275   stomach related diseases. In 1993, (Yeşilada et al., 1993) based on ethnobotanical data, tested

276   this species for its antiulcerogenic activity, and showed that the chloroform fraction of *C.*

277   *solstitialis* exerts remarkable anti-*Helicobacter pylori* activity against both standard strain and

278   clinical isolates at very low concentrations. *H. pylori* is a bacteria which causes ulcers, gastritis

279   and cancer (Covacci et al., 1999).

280   The sesquiterpene lactones have been identified as the active constituents of the chloroform

281   extract of the flowering aerial parts of the plant (especially chlorojanerin and 13-acetyl

282   solstitialin A), and have been isolated through bioassay-guided fractionation procedures

283   (Yesilada et al., 2004). A more recent study has revealed that each of the active compounds

284 possesses a different anti-ulcer activity profile that interacts together in the plant remedy and

285 show a remarkable effect (Gürbüz & Yesilada, 2007).

286 *Antiviral and antimicrobial*

287 *Centaurea solstitialis* has been tested for antimicrobial activity and has shown high activity

288 against *Staphylococcus aureus* at a 0.5 mg/ml concentration. Therefore, *C. solstitialis* may be

289 used as an antibiotic for *S. aureus* infections (Tekeli et al., 2011). (Lograda, T., Ramdani, M.,

290 Chalard, P., Figueredo, G., Khalfoune, K. Silini, 2013) tested the biological activity of the

291 essential oil of *C. solstitialis* grown in Algeria against nine bacterial strains, and it showed

292 moderate to significant antibacterial activity.

293 The sesquiterpenic lactones centaurepensin, chlorojanerin and 13-acetyl solstitialin have been

294 found to accelerate the healing process of labial and genital herpes lesions, providing scientific

295 support for the utilization of *C. solstitialis* against herpes labialis infections in infants in Turkish

296 folk medicine (Özçelik et al., 2009).

297 *Antinociceptive and antipyretic*

298 (Akkol et al., 2009) obtained ethanol and aqueous extracts from the aerial parts and roots of *C.*

299 *solstitialis* and tested it for antinociceptive effects using p-benzoquinone-induced writhing model

300 in mice as a common *in vivo* activity assessment model. The ethanol extracts obtained from both

301 aerial parts and roots showed significant antinociceptive activity, but the activity of the aerial

302 parts was more prominent and close to that of the reference compound acetyl salicylic acid.

303 Hexane and chloroform fractions exerted a potent antinociceptive activity, while n-butanol and

304 remaining aqueous fractions were not significantly active. The ethanol extract of the aerial part

305 also demonstrated a potent antipyretic activity, although less potent then acetyl salicylic acid.

306   *Antiproliferative*

307   (Erenler et al., 2015) isolated two sesquiterpene lactones, solstitialin A and 15-dechloro-15-

308   hydroxychlorojanerin, from the methanol extract of *C. solstitialis* stem and studied the anticancer

309   activities of both compounds. The compounds exhibited significant anticancer activities against

310   HeLa (Human uterus carcinoma) and C6 (Rat Brain tumor) cell lines in different concentrations.

311   The stem extract was preferred for bioassay-guided isolation due to the highest activity. High

312   activity was recorded even in lower concentrations (from 75 µg/mL to 5 µg/mL) for C6 cell

313   lines. However, solstitialin A exhibited low activity at the concentration of 30 µg/mL against

314   HeLa cell lines and did not show any activity at lower concentrations of 20, 10 and 5 µg/mL.

315   **Toxicity studies**

316   The first study on the toxicity of *C. solstitialis* was carried out in 1954, triggered by the

317   emergence of a disease affecting horses in central and northern California, locally known as

318   "chewing disease" or "yellow star thistle poisoning", identified by scientists as "nigropallidal

319   encephalomalacia". The symptoms were abnormal movement disorders which resemble those of

320   Parkinson's disease in humans. It was demonstrated that this disease is linked to the ingestion of

321   large amounts of *C. solstitialis* (Cordy, 1954). Aqueous-ethanolic extracts of the plant have been

322   proven to be toxic to rats, mice and monkeys in moderate dosages (Mettler, F. A., Stern, 1963).

323   Some authors have identified and isolated (through a bioactivity-guided fractionation approach)

324   some neurotoxic sesquiterpenoids from *C. solstitialis* which may be responsible for causing the

325   disease in horses. (Cassady et al., 1979) identified centaurepsin as a cytotoxic constituent.

326   (Stevens, Riopelle & Wong, 1990) isolated repin from *C. solstitialis* plants, which is considered

327   to be the major neurotoxic compound. (Wang et al., 1991) found out that, among the compounds

328   isolated during the study, 13-0-acetylsolstitialin A and cynaropicrin exhibited neurotoxic activity

329   against cultured rat foetal brain cells depending on the concentration. These results have also

330   been supported by (Cheng et al., 1992). (Hay et al., 1994) showed that the toxicity of these

331   sesquiterpene lactones is due to the reactive α-methylene function. (Roy, Peyton & Spencer,

332   1995) isolated and characterized aspartic acid and glutamic acid as two potent neuroexcitotoxic

333   compounds, being aspartic acid the main toxic component in the alcoholic extract of the plant.

334   (Moret et al., 2005) obtained a complete profile of the free nitrogenous fraction of *C. solstitialis*

335   through HPLC procedures and found no particularly high amounts of excitotoxic amino acids in

336   polar extracts of the plant. Tyramine was identified as the most important biologically active

337   amine present in *C. solstitialis*, and the authors suggest that the prolonged consumption of the

338   tyramine containing plant may be, at least partially, responsible for toxic effects observed in

339   horses, but further investigation is needed.

340

341   **Conclusions**

342   The ethnobotanical literature available for the model invasive weed yellow star-thistle showed a

343   diversified range of traditional uses including medicinal, gastronomic, and as prime material,

344   conferring an important economic and cultural value to the species in its native range. However,

345   the only confirmed use of the species in the non-native range was honey-making and, indirectly,

346   as forage, but only within the context of planned weed-control interventions.

347   Traditional knowledge is the consequence of *in-situ* experimentation in the native range of this

348   species for at least several millennia. Of the numerous traditional uses of *C. solstitialis* in its

349   native range the medicinal uses are the most representative, with 16 different specific uses for a

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350 range of medical procedures and conditions, including as antiseptic. Interestingly for a plant

351 considered to be medicinal, the species is also considered a culinary ingredient across several

352 countries of the native range. However, more than half of the ethnobotanical studies which

353 mention *C. solstitialis* had been carried out in Turkey, its ancestral range and its center of

354 speciation, and thus where the species has been present for the longest. Other countries in what is

355 considered the "expanded" native range of the species across the Western Mediterranean,

356 including Italy, have fewer records of medicinal uses even though, curiously, there were more

357 studies reporting its use as a food ingredient in Italy than in Turkey. This exemplifies how

358 number of studies, *per se*, might be an imperfect indicator of actual use, as the choice of what to

359 study must be biased by regional differences in cultural interests. Regardless, we observed a

360 gradient within the native range with numerous and diverse ethnobotanical uses in the ancestral

361 native range of the Eastern Mediterranean and Western Asia, where the species first originated,

362 and gradually less frequent uses as we move towards the expanded native range on the Western

363 Mediterranean. Medicinal uses seem to be particularly slow to be transmitted even within the

364 native range, with most studies of such kind concentrated in the ancestral range of the

365 Mediterranean west, and gradually less reports as we go east, with no uses reported for e.g.,

366 Spain, where it is also considered a native weed.

367 Pharmacological studies have provided support to most of the medicinal uses of the species,

368 confirming that the species contains chemicals that possess antiviral, antimicrobial, antipyretic,

369 antinociceptive, antiulcerogenic, antioxidant, and antiproliferative properties, and that plants

370 from the native range present a richer variety of pharmaceutically active compounds than plants

371 from the non-native range. Invasive plants frequently use active chemical compounds are as

372 chemical defenses against predators, herbivores, and pathogens which are expected to be more

373   abundant in the native than in the non-native range (Liu & Stiling, 2006; Correia et al., 2016).

374   These defenses can be qualitative quantitative (digestibly reducers) to deter specialist herbivores,

375   or qualitative (toxins) to deter generalists (Müller-Schärer, Schaffner & Steinger, 2004).

376   Qualitative chemical defenses (frequently alkaloids) are the ones conferring plants most

377   medicinal properties, but the amount of these chemicals is dependent on genetic and

378   environmental factors, and are known to vary geographically (Sotes et al., 2015; Irimia et al.,

379   2019). The Shifting Defense Hypothesis (Joshi & Vrieling, 2005) poses that when an exotic plant

380   is introduced into a new region where specialist herbivores are frequently absent, plants

381   experience selective pressures to increase the amount of qualitative defenses in these non-native

382   regions (e.g. alkaloids). This directly links with the disproportionate success that these chemical

383   defenses, which might be new to the recipient communities, confer to some invasive species, in

384   what is known as the Novel Weapons Hypothesis (Callaway & Ridenour, 2004). Studies with

385   our model species suggest that novel weapons might contribute to its success in the regions that

386   they invade, but also provide evidence for higher concentration of qualitative defenses in the

387   non-native range of the species, in the form of pharmaceutically active sesquiterpene lactones,

388   paralleled by a reduction in quantitative defenses (Sotes et al., 2015). Thus, on one side we find a

389   richer chemical diversity in the native range of the species, which might contribute to explain the

390   abundant ethnobotanical uses described there, but on the other hand the concentration of

391   pharmaceutically active compounds is higher in at least some non-native regions, which shows

392   potential for ethnobotanical uses yet to be discovered in these invaded areas. Within the native

393   range, we did observe a decrease in both chemical richness and reported ethnobotanical uses as

394   we went from the Mediterranean west to the east, however, this could be a confounding factor

395   that does not necessarily imply that ethnobotanical uses are less frequent because of a lower

396 chemical diversity, since a shorter historical exposure to the plant could also be playing an

397 important role. Our review highlights both the importance of chemical biogeography and the

398 long times involved in the discovery and transmission of cultural plant uses.

399 The lack of transmission of cultural knowledge to the non-native regions of the species is in

400 striking difference with the well documented transmission of ethnobotanical knowledge across

401 continents during significant human migrations. For instance during the European colonization

402 of the Americas abundant ethnobotanical knowledge was brought from West Africa and the

403 Mediterranean, when migrants either brought with them both plants of interest and the

404 knowledge of how to use them, or were able to find substitutes with similar uses in the new

405 colonies (Moret, 2013; Voeks & Rashford, 2013). This has also been documented in reverse, and

406 Colombian migrants have been documented to bring ethnobotanical remedies from America into

407 the UK (Ceuterick et al., 2008). In contrast, our work shows how biological introductions which

408 are not paralleled by significant human migrations can result in a predictably negligible cultural

409 transmission, but also on a very slow local discovery and development of cultural uses.

410 Acknowledgely, we might have missed cultural uses that are not reported in scientific literature,

411 but our methodology was applied coherently among the native and non-native ranges of the

412 species, and there is no reason to expect that any of the studied regions would have a larger

413 amount of scientific literature. If anything, we could expect more studies in the USA, where we

414 could not find any use beyond honey making. Interestingly, even within the native range of the

415 species, different types of ethnobotanical knowledge were transmitted at significantly different

416 rhythms, being particularly slow for medicinal uses and possibly slightly faster for culinary uses.

417 Plant invasions are unplanned experiments that allow us to study the ecological and evolutionary

418 processes unfolding during the colonization of new regions (Hierro, Maron & Callaway, 2005;

419   Montesinos, 2021), our results show how they can also be used as models that allow us to

420   understand, in real time, how ethnobotanical culture is created and transmitted.

421   Overall, our review exemplifies the usefulness of reviews of the ethnobotanic literature about

422   specific invasive taxa. The ancestral range of the invasive weed *C. solstitialis* was where the

423   most numerous and diverse ethnobotanical uses had been described, and are also the regions

424   holding the highest chemical and functional diversity. In the non-native regions the species over-

425   abundance is resulting in significant environmental and economic problems, but also in some

426   incipient economic and cultural activity, such as honey production. As an emerging insight, our

427   work showcases the slow process of cultural integration of exotic species into daily uses,

428   particularly when biological introductions are not accompanied by significant human migrations.

429

430 References

431   Akkol EK, Arif R, Ergun F, Yesilada E. 2009. Sesquiterpene lactones with antinociceptive and antipyretic

432   activity from two Centaurea species. *Journal of Ethnopharmacology* 122:210–215. DOI:

433   10.1016/j.jep.2009.01.019.

434   Andrada AC, Telleria MC. 2005. Pollen collected by honey bees (Apis mellifera L.) from south of Calden

435   district (Argentina): botanical origin and protein content. *Grana*.

436   Beck JJ, Smith L, Merrill GB. 2008. In situ volatile collection, analysis, and comparison of three Centaurea

437   species and their relationship to biocontrol with herbivorous insects. *Journal of Agricultural and*

438   *Food Chemistry*. DOI: 10.1021/jf073383u.

439   Bennett BC, Prance GT. 2000. Introduced plants in the indigenous Pharmacopoeia of Northern South

440   America. *Economic Botany* 54:90–102. DOI: 10.1007/BF02866603.

441 Binder RG, Turner CE, Flath RA. 1990. Comparison of Yellow Starthistle Volatiles from Different Plant

442   Parts. *Journal of Agricultural and Food Chemistry* 38:764–767. DOI: 10.1021/jf00093a038.

443 Birtchnell, M. J., Gibson M. 2008. Flowering ecology of honey-producing flora in south-east Australia.

444   *Rural Industries Research and Development Corporation (Australia)*.

445 Buttery RG, Maddox DM, Light DM, Ling LC. 1986. Volatile Components of Yellow Starthistle. *Journal of*

446   *Agricultural and Food Chemistry* 34:786–788. DOI: 10.1021/jf00071a004.

447 Callaway RM, Cipollini D, Barto K, Thelen GC, Hallett SG, Prati D, Stinson K, Klironomos J. 2008. Novel

448   weapons: invasive plant suppresses fungal mutualists in America but not in its native Europe.

449   *Ecology* 89:1043–55.

450 Callaway RM, Maron JL. 2006. What have exotic plant invasions taught us over the past 20 years ?

451   *Trends in Ecology and Evolution* 21:369–374. DOI: 10.1016/j.tree.2006.04.008.

452 Callaway RM, Ridenour WM. 2004. Novel weapons: invasive success and the evolution of increased

453   competitive ability. *Frontiers in Ecology and the Environment* 2:436–443. DOI: 10.1890/1540-

454   9295(2004)002[0436:NWISAT]2.0.CO;2.

455 Carev I, Ruščić M, Skočibušić M, Maravić A, Siljak-Yakovlev S, Politeo O. 2017. Phytochemical and

456   Cytogenetic Characterization of Centaurea solstitialis L. (Asteraceae) from Croatia. *Chemistry*

457   *and Biodiversity* 14. DOI: 10.1002/cbdv.201600213.

458 Cassady JM, Abramson D, Cowall P, Chang CJ, McLaughlin JL, Aynehchi Y. 1979. Centaurepensin: A

459   cytotoxic constituent of centaurea solstitialis and c. repens (asteraceae). *Journal of Natural*

460   *Products*. DOI: 10.1021/np50004a013.

461 Cassady JM, Hokanson GC. 1978. 3α, 16α-Dihydroxytaraxene-3-acetate: A new triterpene from

462   Centaurea solstitialis. *Phytochemistry*. DOI: 10.1016/S0031-9422(00)94180-3.

463   Ceuterick M, Vandebroek I, Torry B, Pieroni A. 2008. Cross-cultural adaptation in urban ethnobotany:

464   The Colombian folk pharmacopoeia in London. *Journal of Ethnopharmacology* 120:342–359.

465   DOI: 10.1016/j.jep.2008.09.004.

466   Cheng CHK, Costall B, Hamburger M, Hostettmann K, Naylor RJ, Wang Y, Jenner P. 1992. Toxic effects of

467   solstitialin a 13-acetate and cynaropicrin from Centaurea solstitialis L. (asteraceae) in cell

468   cultures of foetal rat brain. *Neuropharmacology*. DOI: 10.1016/0028-3908(92)90177-Q.

469   Cordy DR. 1954. Nigropallidal encephalomalacia in horses associated with ingestion of yellow star

470   thistle. *Journal of neuropathology and experimental neurology*:330–342.

471   Correia M, Montesinos D, French K, Rodríguez-Echeverría S. 2016. Evidence for enemy release and

472   increased seed production and size for two invasive Australian acacias. *Journal of Ecology*

473   104:1391–1399. DOI: 10.1111/1365-2745.12612.

474   Covacci A, Telford JL, Del Giudice G, Parsonnet J, Rappuoli R. 1999. Helicobacter pylori virulence and

475   genetic geography. *Science*. DOI: 10.1126/science.284.5418.1328.

476   DiTomaso JM. 2001. Element stewardship abstract: Centaurea solstitialis L. *Weeds on the Web: The*

477   *Nature Conservancy Wildland Invasive Species Program*.

478   E. Farouji A&, Khodayari H. 2016. Ethnomedicinal plants of Farouj district, North Khorasan province,

479   Iran. *Journal of Herbal Drugs (An International Journal on Medicinal Herbs)*:21–36.

480   Eagle AJ, Eiswerth ME, Johnson WS, Schoenig SE, Cornelis van Kooten G. 2007. Costs and Losses Imposed

481   on California Ranchers by Yellow Starthistle. *Rangeland Ecology & Management* 60:369–377.

482   DOI: 10.2111/1551-5028(2007)60[369:CALIOC]2.0.CO;2.

483   Enders M, Havemann F, Ruland F, Bernard-Verdier M, Catford JA, Gómez-Aparicio L, Haider S, Heger T,

484   Kueffer C, Kühn I, Meyerson LA, Musseau C, Novoa A, Ricciardi A, Sagouis A, Schittko C, Strayer

485   DL, Vilà M, Essl F, Hulme PE, van Kleunen M, Kumschick S, Lockwood JL, Mabey AL, McGeoch

486   MA, Palma E, Pyšek P, Saul WC, Yannelli FA, Jeschke JM. 2020. A conceptual map of invasion

487   biology: Integrating hypotheses into a consensus network. *Global Ecology and Biogeography*

488   29:978–991. DOI: 10.1111/geb.13082.

489 Erenler R, Sen O, Sahin Yaglioglu A, Demirtas I. 2015. Bioactivity-Guided Isolation of Antiproliferative

490   Sesquiterpene Lactones from Centaurea Solstitialis L. ssp. Solstitialis. *Combinatorial chemistry &*

491   *high throughput screening*.

492 Eriksen RL, Hierro JL, Eren Ö, Andonian K, Török K, Becerra PI, Montesinos D, Khetsuriani L, Diaconu A,

493   Kesseli R. 2014. Dispersal pathways and genetic differentiation among worldwide populations of

494   the invasive weed Centaurea solstitialis L. (Asteraceae). *PLOS ONE* 9:e114786. DOI:

495   10.1371/journal.pone.0114786.

496 Esmaeili A, Rustaiyan A, Akbari MT, Moazami N, Masoudi S, Amiri H. 2006. Composition of the essential

497   oils of Xanthium strumarium L. and Centaurea solstitialis L. from Iran. *Journal of Essential Oil*

498   *Research* 18:427–429. DOI: 10.1080/10412905.2006.9699131.

499 Garcia-Jacas N, Uysal T, Romashchenko K, Suárez-Santiago VN, Ertugrul K, Susanna A. 2006. Centaurea

500   revisited: a molecular survey of the Jacea group. *Annals of Botany* 98:741–53.

501 Geraci A, Amato F, Di Noto G, Bazan G, Schicchi R. 2018. The wild taxa utilized as vegetables in Sicily

502   (Italy): A traditional component of the Mediterranean diet. *Journal of Ethnobiology and*

503   *Ethnomedicine*. DOI: 10.1186/s13002-018-0215-x.

504 Gerlach JD. 2004. The impacts of serial land-use changes and biological invasions on soil water resources

505   in California, USA. *Journal of Arid Environments*. DOI: 10.1016/S0140-1963(03)00102-2.

506 Grime JP. 1974. Vegetation classification by reference to strategies. *Nature*. DOI: 10.1038/250026a0.

507 Guarrera PM, Lucia LM. 2007. Ethnobotanical remarks on central and southern Italy. *Journal of*

508   *Ethnobiology and Ethnomedicine*. DOI: 10.1186/1746-4269-3-23.

509   Gürbüz I, Yesilada E. 2007. Evaluation of the anti-ulcerogenic effect of sesquiterpene lactones from

510   Centaurea solstitialis L. ssp. solstitialis by using various in vivo and biochemical techniques.

511   *Journal of ethnopharmacology* 112:284–91. DOI: 10.1016/j.jep.2007.03.009.

512   Hay AJB, Hamburger M, Hostettmann K, Hoult JRS. 1994. Toxic inhibition of smooth muscle contractility

513   by plant-derived sesquiterpenes caused by their chemically reactive α-methylenebutyrolactone

514   functions. *British Journal of Pharmacology*. DOI: 10.1111/j.1476-5381.1994.tb13020.x.

515   Hierro JL, Callaway RM. 2003. Allelopathy and exotic plant invasion. *Plant and Soil* 256:29–39. DOI:

516   10.1023/A:1026208327014.

517   Hierro JL, Eren Ö, Khetsuriani L, Diaconu A, Török K, Montesinos D, Andonian K, Kikodze D, Janoian L,

518   Villarreal D, Estanga-Mollica ME, Callaway RM. 2009. Germination responses of an invasive

519   species in native and non-native ranges. *Oikos* 118:529–538. DOI: 10.1111/j.1600-

520   0706.2009.17283.x.

521   Hierro JL, Khetsuriani L, Andonian K, Eren Ö, Villarreal D, Janoian G, Reinhart KO, Callaway RM. 2016.

522   The importance of factors controlling species abundance and distribution varies in native and

523   non-native ranges. *Ecography* 39:1–12. DOI: 10.1111/ecog.02633.

524   Hierro JL, Lortie CJ, Villarreal D, Estanga-Mollica ME, Callaway RM. 2011. Resistance to Centaurea

525   solstitialis invasion from annual and perennial grasses in California and Argentina. *Biological

526   Invasions*:2249–2259. DOI: 10.1007/s10530-011-0037-4.

527   Hierro JL, Maron JL, Callaway RM. 2005. A biogeographical approach to plant invasions : the importance

528   of studying exotics in their introduced and native range. *Journal of Ecology* 93:5–15. DOI:

529   10.1111/j.1365-2745.2004.00953.x.

530   Irimia RE, Hierro JL, Branco S, Sotes G, Cavieres LA, Eren Ö, Lortie CJ, French K, Callaway RM, Montesinos

531   D. 2021. Experimental admixture among geographically disjunct populations of an invasive plant

532   yields a global mosaic of reproductive incompatibility and heterosis. *Journal of Ecology*

533   109:2152–2162. DOI: 10/gh6jtb.

534   Irimia RE, Lopes SMM, Sotes G, Cavieres LA, Eren Ö, Lortie CJ, French K, Hierro JL, Rosche C, Callaway

535   RM, Pinho e Melo TMVD, Montesinos D. 2019. Biogeographic differences in the allelopathy of

536   leaf surface extracts of an invasive weed. *Biological Invasions* 21:3151–3168. DOI:

537   10.1007/s10530-019-02038-1.

538   Jakupovic J, Jia Y, Pathak VP, Bohlmann F, King RM. 1986. Bisabolone derivatives and sesquiterpene

539   lactones from centaurea species. *Planta medica*. DOI: 10.1055/s-2007-969197.

540   Joshi J, Vrieling K. 2005. The enemy release and EICA hypothesis revisited: incorporating the

541   fundamental difference between specialist and generalist herbivores. *Ecology Letters* 8:704–

542   714.

543   Kargioğlu M, Cenkci S, Serteser A, Evliyaoğlu N, Konuk M, Kök MŞ, Baǧci Y. 2008. An ethnobotanical

544   survey of inner-west Anatolia, Turkey. *Human Ecology*. DOI: 10.1007/s10745-008-9198-x.

545   Koc S, Isgor BS, Isgor YG, Shomali Moghaddam N, Yildirim O. 2015. The potential medicinal value of

546   plants from Asteraceae family with antioxidant defense enzymes as biological targets.

547   *Pharmaceutical Biology*. DOI: 10.3109/13880209.2014.942788.

548   Lentini F, Venza F. 2007. Wild food plants of popular use in Sicily. *Journal of ethnobiology and*

549   *ethnomedicine* 3:15.

550   Licata M, Tuttolomondo T, Leto C, Virga G, Bonsangue G, Cammalleri I, Gennaro MC, La Bella S. 2016. A

551   survey of wild plant species for food use in Sicily (Italy) - results of a 3-year study in four

552   Regional Parks. *Journal of Ethnobiology and Ethnomedicine*. DOI: 10.1186/s13002-015-0074-7.

553   Liu H, Stiling P. 2006. Testing the enemy release hypothesis: a review and meta-analysis. *Biological*

554   *Invasions* 8:1535–1545. DOI: 10.1007/s10530-005-5845-y.

555   Lograda, T., Ramdani, M., Chalard, P., Figueredo, G., Khalfoune, K. Silini H. 2013. Phyto-chemistry,

556   antibacterial activity and chromosome number of Centaurea solstitialis L. grown in Algeria.

557   *Global Journal of Research on Medicinal Plants & Indigenous Medicine*:675.

558   Maddox DM, Mayfield A, Poritz NH. 1985. Distribution of yellow starthistle (Centaurea solstitialis) and

559   russian knapweed (Centaurea repens). *Weed Science* 33:315–327.

560   Masso, J. L., Bertran, M. N., Adzet T. 1979. Contribution to the chemical and pharmacological study of

561   some species of Centaurea. *Plantes Medicinales et Phytotherapie*:41–45.

562   Merrill GB, Stevens KL. 1985. Sesquiterpene lactones from Centaurea solstitialis. *Phytochemistry*. DOI:

563   10.1016/S0031-9422(00)83113-1.

564   Mettler, F. A., Stern GM. 1963. Observations on the toxic effects of yellow star thistle. *Journal of*

565   *neuropathology and experimental neurology*:164–169.

566   Montesinos D. 2021. Fast invasives fastly become faster: Invasive plants align largely with the fast side of

567   the plant economics spectrum. *Journal of Ecology*:1365-2745.13616. DOI: 10.1111/1365-

568   2745.13616.

569   Moret ES. 2013. Trans-atlantic diaspora ethnobotany: Legacies of west African and iberian

570   mediterranean migration in central Cuba. In: *African Ethnobotany in the Americas*. Springer New

571   York, 217–245. DOI: 10.1007/978-1-4614-0836-9_9.

572   Moret S, Populin T, Conte LS, Cosens G. 2005. HPLC determination of free nitrogenous compounds of

573   Centaurea solstitialis (Asteraceae), the cause of equine nigropallidal encephalomalacia. *Toxicon*.

574   DOI: 10.1016/j.toxicon.2005.07.006.

575   Müller-Schärer H, Schaffner U, Steinger T. 2004. Evolution in invasive plants: implications for biological

576   control. *Trends in Ecology and Evolution* 19:417–422. DOI: 10.1016/j.tree.2004.05.010.

577   Naab OA, Tamame MA, Caccavari MA. 2008. Palynological and physicochemical characteristics of three

578   unifloral honey types from central Argentina. *Spanish Journal of Agricultural Research* 6:566–

579   576.

580   Nuñez MA, Kuebbing S, Dimarco RD, Simberloff D. 2012. Invasive Species: To eat or not to eat, that is the

581   question. *Conservation Letters*. DOI: 10.1111/j.1755-263X.2012.00250.x.

582   Oster M, Beck JJ, Furrow RE, Yeung K, Field CB. 2015. In-field yellow starthistle (Centaurea solstitialis)

583   volatile composition under elevated temperature and CO2and implications for future control.

584   *Chemoecology*. DOI: 10.1007/s00049-015-0200-y.

585   Özçelik B, Gürbüz I, Karaoglu T, Yeşilada E. 2009. Antiviral and antimicrobial activities of three

586   sesquiterpene lactones from Centaurea solstitialis L. ssp. solstitialis. *Microbiological Research*

587   164:545–552. DOI: 10.1016/j.micres.2007.05.006.

588   Persano Oddo L, Piana L, Bogdanov S, Bentabol A, Gotsiou P, Kerkvliet J, Martin P, Morlot M, Ortiz

589   Valbuena A, Ruoff K, von der Ohe K. 2004. Botanical species giving unifloral honey in Europe.

590   *Apidologie*. DOI: 10.1051/apido:2004045.

591   Roy DN, Peyton DH, Spencer PS. 1995. Isolation and identification of two potent neurotoxins, aspartic

592   acid and glutamic acid, from yellow star thistle (Centaurea solstitialis). *Natural Toxins*. DOI:

593   10.1002/nt.2620030309.

594   Schaffner U, Ridenour WM, Wolf VC, Bassett T, Müller C, Müller-Schärer H, Sutherland S, Lortie CJ,

595   Callaway RM. 2011. Plant invasions, generalist herbivores, and novel defense weapons. *Ecology*

596   92:829–835. DOI: 10.1890/10-1230.1.

597   Şen A, Bitiş L, Birteksöz-Tan S, Bulut G. 2013. In vitro evaluation of antioxidant and antimicrobial

598   activities of some Centaurea L. species. *Marmara Pharmaceutical Journal*. DOI:

599   10.12991/201317391.

600 Senatore F, Formisano C, Raio A, Bellone G, Bruno M. 2008. Volatile components from flower-heads of

601   Centaurea nicaeensis All., C. parlatoris Helder and C. solstitialis L. ssp. schouwii (DC.) Dostál

602   growing wild in southern Italy and their biological activity. *Natural Product Research* 22:825–

603   832. DOI: 10.1080/14786410500410719.

604 Somerville DC. 2005. Lipid content of honey bee-collected pollen from south-east Australia. *Australian*

605   *Journal of Experimental Agriculture* 45:1659–1661. DOI: 10.1071/EA03190.

606 Sotes GJ, Cavieres LA, Montesinos D, Pereira Coutinho AX, Peláez WJ, Lopes SMM, Pinho e Melo TMVD.

607   2015. Inter-regional variation on leaf surface defenses in native and non-native Centaurea

608   solstitialis plants. *Biochemical Systematics and Ecology* 62:208–218. DOI:

609   10.1016/j.bse.2015.09.003.

610 Stepp JR, Moerman DE. 2001. The importance of weeds in ethnopharmacology. *Journal of*

611   *Ethnopharmacology* 75:19–23. DOI: 10.1016/S0378-8741(00)00385-8.

612 Stevens KL, Riopelle RJ, Wong RY. 1990. Repin, a sesquiterpene lactone from acroptilon repens

613   possessing exceptional biological activity. *Journal of Natural Products*. DOI:

614   10.1021/np50067a038.

615 Tekeli Y, Zengin G, Aktumsek A, Sezgin M, Torlak E. 2011. Antibacterial activities of extracts from twelve

616   Centaurea species from Turkey. *Archives of Biological Sciences*. DOI: 10.2298/ABS1103685T.

617 Thiessen WE, Hope H. 1969. The structure and absolute configuration of solstitialin, C15H20O5. *Acta*

618   *Crystallographica Section B: Structural Crystallography and Crystal Chemistry*:554–562.

619 Thomsen CD, Williams WA, Vayssiéres M, Bell FL, George MR. 1993. Controlled grazing on annual

620   grassland decreases yellow starthistle. *California Agriculture*.

621 Voeks R, Rashford J. 2013. *African ethnobotany in the Americas*. Springer New York. DOI: 10.1007/978-1-

622   4614-0836-9.

623   Wang Y, Hamburger M, Cheng CHK, Costall B, Naylor RJ, Jenner P, Hostettmann K. 1991. Neurotoxic

624   Sesquiterpenoids from the Yellow Star Thistle Centaurea solstitialis L. (Asteraceae). *Helvetica*

625   *Chimica Acta*. DOI: 10.1002/hlca.19910740114.

626   Xiao S, Callaway RM, Graebner R, Hierro JL, Montesinos D. 2016. Modeling the relative importance of

627   ecological factors in exotic invasion: The origin of competitors matters, but disturbance in the

628   non-native range tips the balance. *Ecological Modelling* 335:39–47. DOI:

629   10.1016/j.ecolmodel.2016.05.005.

630   Yesilada E, Gürbüz I, Bedir E, Tatli I, Khan I a. 2004. Isolation of anti-ulcerogenic sesquiterpene lactones

631   from Centaurea solstitialis L. ssp. solstitialis through bioassay-guided fractionation procedures in

632   rats. *Journal of ethnopharmacology* 95:213–9. DOI: 10.1016/j.jep.2004.07.021.

633   Yeşilada E, Sezik E, Fujita T, Tanaka S, Tabata M. 1993. Screening of some Turkish medicinal plants for

634   their antiulcerogenic activities. *Phytotherapy Research*. DOI: 10.1002/ptr.2650070313.

635   Zouhar Kris. 2002. Centaurea solstitialis. In: Fire Effects Information System, [Online]. *U.S. Department of*

636   *Agriculture, Forest Service, Rocky Mountain Research Station, Fire Sciences Laboratory*

637   *(Producer)*.

Figure 1

Figure 1

Number of articles by geographical origin, within the native range.
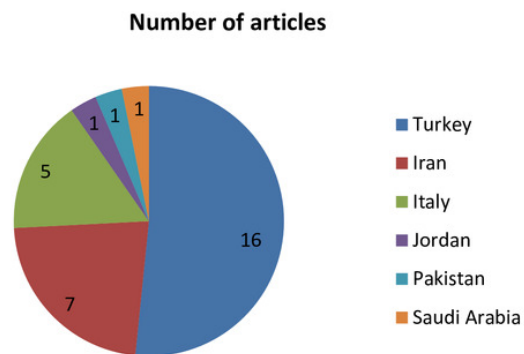
Figure 1. Number of articles by geographical origin, within the native range.

Figure 2

Figure 2

Number of studies reporting different ethnobotanical uses across countries. Honey making is not shown for the native range as it is common throughout.

Figure 2. Number of studies reporting different ethnobotanical uses across countries. Honey making is not shown for the native range as it is common throughout.
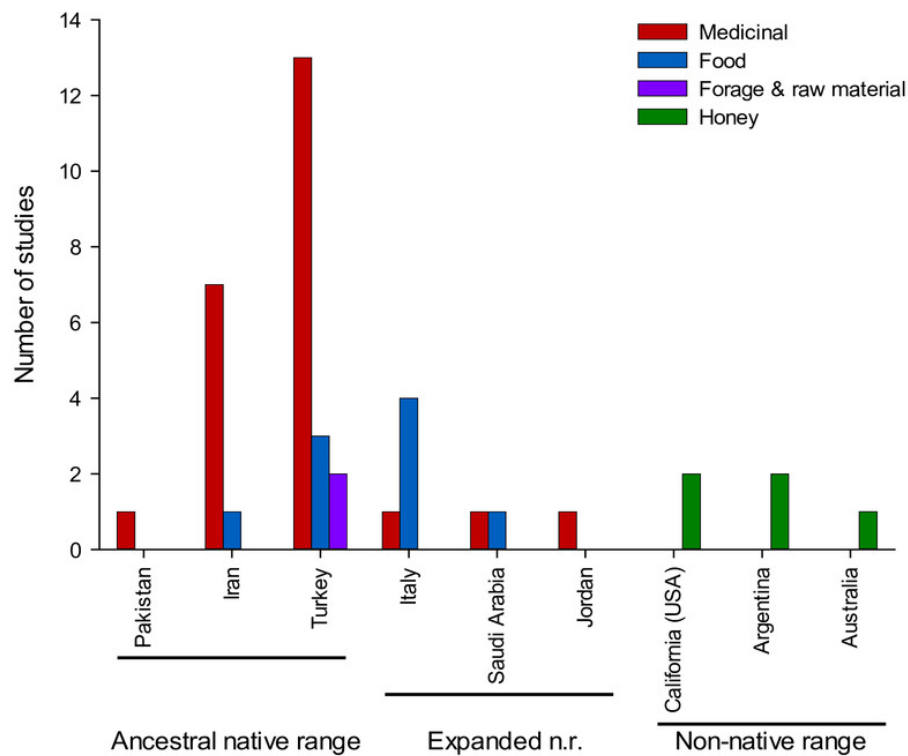
Figure 3

Figure 3

Number of compounds that have been identified exclusively in one region.

Figure 3. Number of compounds that have been identified exclusively in one region.
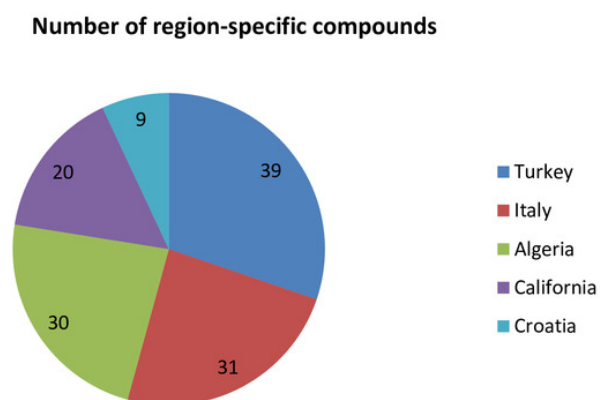
Figure 4

Figure 4

Number of compounds found exclusively in the native range.

Figure 4. Number of compounds found exclusively in the native range
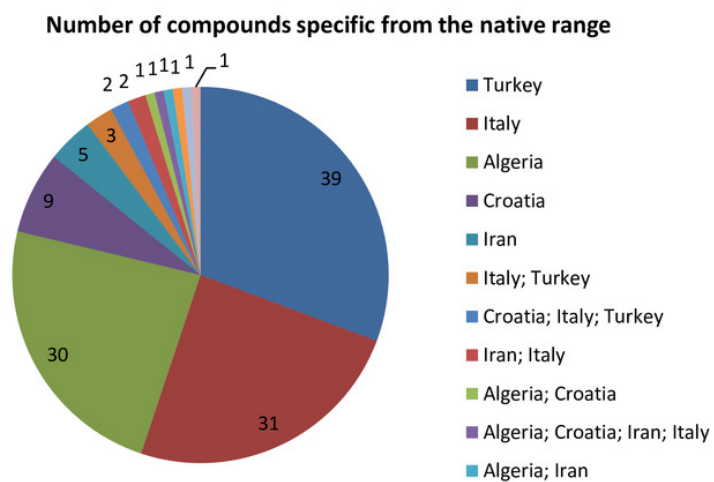
Figure 5

Figure 5

Diversity of terpene and nonterpene compounds per region.

Figure 5. Diversity of terpene and nonterpene compounds per region