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1 **Final version of manuscript submitted to Economic Botany**

2 **Cross-cultural comparison of medicinal plants used to treat infections in northern**

3 **Thailand**

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18

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23 Drug resistance in pathogenic microorganisms threatens both human and animal health.
24 This has prompted the search for new antimicrobial drugs, including ones from plant-
25 derived medicines. Some researchers have suggested that medicinal plants used by
26 multiple cultures are more likely to be pharmacologically active. We interviewed 808
27 informants across seven ethnic groups in northern Thailand about their traditional
28 knowledge of medicinal plants. Plants used to treat infections were compared and
29 agreement about a particular use of a plant was evaluated using the “frequency of citation.”
30 When agreements were found between two or more informants, we searched for
31 confirmation in other studies for medicinal uses and biological activities reported for that
32 particular plant species. Of the 808 informants, 103 mentioned 199 distinct plant uses of
33 143 plant species to treat 21 different “infection” disorders. Of the 199 plant uses, 114
34 were mentioned by two or more informants; 15 plant uses were shared between different
35 ethnic groups and 55 plant uses were shared within the same ethnic group and had identical
36 or similar uses mentioned in other studies sometimes in distantly located cultures. The
37 convergent information suggests the bioactivity of a certain plant that may have been
38 discovered independently. However, the remaining 44 plant uses that were shared within
39 the same ethnic group are here reported for the first time with considerable agreement
40 among informants. These new plant uses should be given high priority in bioscreening for
41 new antimicrobial drugs.

42 Thai Abstract?

43 **Key Words:** Antimicrobial resistance; Antimicrobial activity; Ethnobotany;

44 Ethnomedicine; New drug discovery; Traditional medicine

45

46 **Introduction**

47

48 Infectious diseases are caused by pathogenic microorganisms and they can be classified based
49 on pathogens causing the infections, i.e., bacterial, parasitic, viral, and fungal diseases,
50 respectively. Infectious diseases have become a major threat to humans, and, at the same time,
51 growing resistance to pharmaceutical drugs increasingly threatens the effective prevention and
52 treatment of diseases caused by microorganisms (Pommerville 2014; WHO 2016). Colistin is the
53 last resort for treating life threatening infections caused by Enterobacteriaceae, a family of Gram-
54 negative bacteria that includes many familiar pathogens, such as *Escherichia coli* and *Yersinia*
55 *pestis*. Recently the World Health Organization reported that resistance to colistin has been
56 detected in several countries. Antibiotic resistance is present in all countries, in some cases,
57 affecting more than half of the patients. In many European countries, as well as in Japan and
58 South Africa, there have been failures in the treatment with the last resort of medicine for
59 gonorrhea (third generation cephalosporin antibiotics) caused by emerging new resistance
60 mechanisms of the bacteria. Such new resistance mechanisms have also been detected in
61 tuberculosis, HIV, influenza, malaria, and many other infectious diseases (WHO 2016). In
62 addition to occurring in microorganisms, drug resistance is also found in gastrointestinal
63 helminthes in humans and animals (Saddiqe et al. 2013). Therefore, new antimicrobial drugs and
64 anthelmintics are needed. One potential source of new drugs is traditional plant-derived
65 medicines (Namita and Mukesh 2012).

66 According to the WHO, about three-quarters of the world's population depends on
67 traditional herbal medicine for their health care needs (Gilani and Rahman 2005). There have

68 been efforts to duplicate the effective traditional medicine used by traditional healers to develop
69 new western anti-infection medicine (Vijayakumar et al. 2016).

70 Documented ethnomedical systems (e.g., Ayurveda, Traditional Chinese Medicine,
71 Unani Tibb) and non-documented traditional medicine of different ethnic groups (i.e.,
72 ethnomedicine) are seen as valuable short-cuts in the search for and selection of candidate plant
73 species for screening of biologically active compounds for new drug discovery (Cowan 1999;
74 Katiyar et al. 2013; Schultes 1994). The history of drug discovery and development confirms that
75 ethnomedicinal-based screening of floras have a higher chance of success than a random
76 screening approach (Albuquerque 2010; Cox and Balick 1994). Significant examples of
77 successful drug discovery based on ethnomedicinal usage by indigenous people or folk
78 medicinal system include the discovery of quinine from the bark of *Cinchona* (*Cinchona*
79 *pubescens* Vahl) for treating malaria, reserpine from the Indian snake root (*Rauwolfia serpentina*
80 (L.) Benth. ex Kurz) for treating hypertension, and morphine and codeine from the opium poppy
81 (*Papaver somniferum* L.) for treating pain (Cox and Balick 1994; Williams 2006).

82 To increase hit rates in phytomedicinal exploration, researchers have used ethnobotanical
83 indices, which incorporate the number of uses, persistence of use over time, frequency of use,
84 and agreement about use (Saslis-Lagoudakis et al. 2011; Tardío and Pardo-de-Santayana 2008).
85 Besides the use of ethnobotanical indices, other mathematical techniques including comparison
86 of plant uses can also help to validate the use of a species for a particular use (e.g., Bennett and
87 Husby 2008; Bletter 2007). Use of one species for the same purpose in different cultures may be
88 due to knowledge transfer or independent discovery (Bletter 2007). The latter is more likely with
89 greater linguistic differences and greater geographic differences (Johnson 2006). Agreement on
90 use across cultures may increase the probability of therapeutic efficacy (Bletter 2007; Heinrich et

91 al. 1998; Saslis-Lagoudakis et al. 2011). For instance, Roersch (2010) reviewed the
92 ethnomedicinal uses of *Piper umbellatum* L. across three continents (America, Africa, Asia) and
93 recorded its traditional use across different cultures in 24 countries and found that it is used with
94 a high degree of cross-cultural consensus (i.e., use for treatment of wounds) which was
95 supported by scientific evidence for the related activities; i.e., antioxidant activity which play an
96 important role in wound healing. Similarly, in small-scale communities (e.g., a village),
97 biological activity (i.e., antibacterial activity) in laboratory test of medicinal plants was
98 correlated with frequency of mention (i.e., citation) of plant use, giving support to the empirical
99 knowledge on plant use of the inhabitants of the community (Hernández et al. 2003).

100 In this study, we compare the medicinal plants used to treat infectious diseases across
101 seven different cultures (i.e., ethnic groups) in northern Thailand; namely, the Tai Yuan (or
102 “Khon Müang” which is their self-designed name), Hmong, Mien (sometimes called “Yao”),
103 Lahu, Lisu, Lua and Khamu (also known as Khmu or Kammu). The Tai Yuan are the main
104 ethnic group and constitute the majority of the population in northern Thailand. The Hmong,
105 Mien, Lahu, and Lisu are ethnic groups that originate in southern China and they were forced to
106 migrate southward into upper Indochina in the 19th century by the invasion and political pressure
107 from the Han Chinese (Perve 2006). The Lua is a sub-group of the Lawa people originating in
108 the areas of Thai-Lao border where they now live, particularly in the mountains in Nan Province
109 (Dessaint 1981). Likewise, the Khamu is a small ethnic group believed to be the aboriginals to
110 northern Laos and surrounding areas. They currently live in Laos, Vietnam, Thailand, China, and
111 the United States (Nguyen et al. 2009). In general, we aimed to determine whether there was
112 agreement in use of a certain plant species among them. For species mentioned for a treatment of
113 particular condition by more than one informant, we searched the literature for similar uses.

114 When that was the case we searched for information about their biological activity, especially
115 whether it had been confirmed in the laboratory.

116

117 <H1>Methods

118

119 <H2>STUDY SITES AND ETHNIC GROUPS

120

121 Data about plants used to treat infections were collected in 16 villages representing seven
122 different cultures (i.e., ethnic groups) in northern Thailand. Twelve of the villages were in Nan
123 Province and four in Chiang Mai Province (Table 1).

124

125 <H2>DATA COLLECTION

126

127 Ethnobotanical surveys were carried out from 2007 to 2011 in Nan Province and from 2014 to
128 2017 in Chiang Mai Province. Data collection followed the technique of ethnobotanical inventory
129 or field interview suggested by Martin (1995). In each village, people with specialist plant
130 knowledge (i.e., traditional healers) were asked for their consent to engage in the study and
131 selected as local key informant(s). Totally, there were 28 key informants who consented to
132 engage in the surveys in the 16 villages (i.e., 1–3 informants per village; Table 1).

133 The surveys of traditional knowledge from local key informants were made every other
134 month in all habitats where we expected to find useful plants, including home gardens, cultivated
135 fields, and nearby forests. The key informants were asked about vernacular names, part used,
136 mode of preparation, and routes of administration of each medicinal plant. The interviews were
137 conducted by the first author in Thai language with the assistance of a translator when the

138 informants were not fluent in Thai. Initial identifications were based on the first author's
139 previous knowledge of the flora. These initial identifications were subsequently confirmed with
140 voucher specimens (81 out of 96 species presented in Appendix 1 - Electronic Supplementary
141 Material, ESM) deposited at the herbarium QBG and with the help of a specialist at the Queen
142 Sirikit Botanical garden (QSBG) in Mae Rim, Chiang Mai, Thailand. Species for which no
143 vouchers were collected were well known cultivated plants, such as, e.g., the papaya (*Carica*
144 *papaya* L.), garlic (*Allium sativum* L.), galangal (*Alpinia galanga* (L.) Willd.), lemongrass
145 (*Cymbopogon citratus* (DC.) Stapf), sugarcane (*Saccharum officinarum* L.), the pantropical weed
146 *Calotropis gigantea* (L.) Dryand., and the ornamental *Aglaonema*, etc. Botanical names of plant
147 species follow The Plant List (The Plant List 2013).

148 After the field surveys with the 28 key informants were completed, all plant species
149 reported as medicinal by the key informant in a given village were subjected to open-ended
150 questionnaire interviews with local residents in each village to determine consensus of their
151 medicinal use(s). We interviewed 780 general informants from the 16 villages, i.e., 60 people per
152 village in Nan Province and 15 people per village in Chiang Mai Province (Table 1). During the
153 interview, pictures of the medicinal plants were shown to each informant to avoid
154 misunderstandings concerning the identity of plant names used. All informants were asked about
155 the medicinal uses of each species for treating health conditions using the same questions as we
156 had asked to the key informants, i.e., none of the informants were guided by medicinal uses
157 mentioned by the key informants but, instead, they were free to mention all medicinal use(s) they
158 knew for a given plant species. Whenever informants, who could not communicate well in Thai
159 language, encountered a problem in not being able to define what the symptom was called in

160 Thai, they were asked to say it in their ethnic language or explain the symptoms to the translator
161 who then translated that into Thai language for the record.

162

163 <H2>DATA ANALYSIS

164

165 Since the ethnobotanical data obtained through the interviews with key informants in the field
166 surveys and questionnaire interviews with general informants were independent, the two data
167 sets were pooled as one dataset. Only data related to the use of medicinal plants to treat
168 infections were compared. The symptoms fit in the category ‘infections’ in the *Economic Botany*
169 *Data Collection Standard* (Cook 1995).

170 The discrete event in which an informant mentions the use of a plant species for the
171 treatment of a particular infective symptom is here defined as a “citation.” To evaluate the degree
172 of agreement among informants concerning the ethnobotanical use of a particular medicinal plant
173 for treating specific infective conditions, we used the term “frequency of citation” (Tardío and
174 Pardo-de-Santayana 2008), i.e., total citation for the species for such use.

175 Plant use data were compared both within and between the studied ethnic groups.
176 Agreement concerning use of plants was therefore categorized into three types; i.e., 1. agreement
177 between different ethnic groups, 2. agreement between different villages inhabited by the same
178 ethnic group; and 3. agreement between informants of the same ethnic group inhabiting the same
179 village. Use of the same plant species by the same route of administration to treat the same
180 infective condition that were mentioned by at least two informants from the same village were
181 grouped as one “combined citation.” All “combined citations” from 16 villages were then
182 compared and grouped based on plant species used to treat the same disorder as one “distinct

183 use”. A “distinct use” of all plant species was also compared with other ethnobotanical studies or
184 the relevant literature for confirmation.

185

186 <H1>Results

187

188 <H2>ETHNOBOTANICAL DATA FOR PLANTS USED TO TREAT INFECTIONS

189

190 One hundred and three informants (40 in Chiang Mai; 63 in Nan) out of 808 informants (28 key-
191 informants, 780 general informants) participating in the field surveys and questionnaire
192 interviews provided 955 citations for 143 plant species from 68 families used to treat 21
193 “infection” disorders. These were grouped into unspecified infection (e.g., fever), helminth worm
194 infections, bacterial infections, viral infections, fungal infections, and protozoal infections (Table
195 2). Common ailments, such as fever, *tinea pedis*, ringworm, cold, chicken pox, and shingles,
196 were the most frequently reported infectious disorders. Medicinal plants were most often used to
197 treat fever (61 spp.), ringworm (21 spp.), *tinea pedis* (20 spp.), and cold (19 spp.), respectively
198 (Table 2).

199

200 <H2>COMPARISON OF MEDICINAL PLANTS USED TO TREAT INFECTIONS

201

202 In total, we counted 186 combined citations (including 870 single citations) relating to 96 plant
203 species for the treatment of 20 different disorders (Table 2) whereas the remaining 85 citations
204 relating to 64 species were reported by a single informant and not shared with others (Table 3).
205 The shared uses were frequently reported for fever, *tinea pedis*, ringworm, chicken pox, and

206 cold, whereas onychomycosis (*tinea unguium*) was the only disorder for which the use
207 mentioned for its treatment was not shared (Table 2).

208 The comparison of 186 combined citations from 16 villages eventually resulted in 114
209 distinct uses, of which 15 were shared between two or more villages inhabited by different ethnic
210 groups (Agreement type 1), 14 were shared between two or more villages inhabited by the same
211 ethnic group (Agreement type 2), and 85 were shared between informants inhabiting the same
212 village (Agreement type 3; Table 3). The 114 distinct uses are detailed in Appendix 1 (ESM)
213 while the details of 85 citations reported by a single informant in a village (i.e., 85 distinct uses)
214 are not shown.

215 Among the 15 distinct uses shared between different ethnic groups, the use of
216 *Strobilanthes cusia* to treat fever showed the highest degree of agreement (96 citations; 11
217 villages; 4 ethnic groups), followed by the use of *Gmelina arborea* Roxb. to treat *tinea pedis* (76
218 citations; 10 villages; 4 ethnic groups), and the use of *Eleusine indica* (L.) Gaertn. to treat fever
219 (38 citations; 6 villages; 4 ethnic groups), respectively (Appendix 1, ESM). For this type of
220 agreement (type 1), four distinct uses related to the treatment of fever were shared between
221 ethnic groups living in different provinces; i.e., *Ageratum conyzoides* (L.) L., *Artemisia vulgaris*
222 L. (Lahu in Chiang Mai and Hmong in Nan), *Eleusine indica* (Khamu and Lua in Nan and Tai
223 Yuan and Hmong in Chiang Mai), and *Mimosa pudica* L. (Mien in Nan and Tai Yuan in Chiang
224 Mai).

225 Of the 14 distinct uses shared between villages inhabited by the same ethnic group, the
226 use of *Toona sinensis* to treat chicken pox by the Hmong showed the highest degree of
227 agreement (35 citations; 3 villages), followed by the use of *Stephania* sp. to treat ringworm by
228 the Mien (19 citations; 3 villages), and *Verbena officinalis* L. to treat *tinea pedis* (18 citations; 3

229 villages), respectively (Appendix 1, ESM). For this type of agreement (type 2), only the use of
230 *Verbena officinalis* to treat *tinea pedis* (athlete's foot) were shared between the Hmong in Nan
231 and Chiang Mai Province whereas the remaining were uses shared between villages of the same
232 ethnic group in Nan Province.

233 Of the 85 distinct uses shared between informants within a village of the same ethnic
234 group, the use of *Toona sinensis* (Juss.) M.Roem. to treat dengue by the Hmong showed the
235 highest degree of agreement (14 citations), followed by the use of *Pseudodrynaria coronans*
236 (Wall. ex Mett.) Ching to treat shingles (12 citations) and *Chromolaena odorata* (L.) R.M.King
237 & H.Rob. to treat fever (11 citations) by the Tai Yuan, and *Dianella ensifolia* (L.) DC. to treat
238 cold by the Lua (10 citations), respectively (Appendix 1, ESM).

239

240 <H2>CONFIRMATION OF MEDICINAL PLANTS USED TO TREAT INFECTIONS

241

242 Comparing the 114 distinct uses with other published studies, we found similarity or associated
243 biological activity for 70 distinct uses. We were unable to find any published evidence for 44
244 distinct uses reported by the informants in this study (Appendix 1, ESM).

245 Among the 70 distinct uses, confirmation was found for all 15 uses shared between
246 ethnic groups (Type 1), 11 uses shared between villages of the same ethnic group (Type 2), and
247 44 uses shared between informants in a village of the same ethnic group (Type 3). Most uses
248 were corroborated by surveys of medicinal plants or ethnobotanical studies in Thailand, other
249 Asian countries such as China, Laos, India, Pakistan, Bangladesh, Philippines, Malaysia, and
250 Indonesia as well as some distant countries such as the United States, Jamaica, Nigeria, Trinidad,
251 Cameroon, Mauritius, and Zimbabwe. Besides, the confirmation included some studies focussed

252 on particular plant species to verify their anti-infection activity (see Appendix 2, ESM). Sixty of
253 those were corroborated by reports of use of the same plant species for treating the same
254 disorders as documented here or by the confirmation of pharmacological activity of the same
255 plant, three were corroborated by the reports to congeneric species used to treat the same
256 disorders [i.e., *Selaginella* species for treating hepatitis (Setyawan 2009, 2011; Wang et al. 1998)
257 vs. *Selaginella willdenowii* (Desv. ex Poir.) Baker; *Toona ciliata* M.Roem. for treating fever
258 (Hossain et al. 2014) vs. *Toona sinensis*, and *Artemisia vulgaris* for treating fever (Ong and Kim
259 2014; Spring 1989) vs. *Artemisia verlotiorum* Lamotte], and seven were corroborated by the
260 reports of the same plant species for treating disorders similar to what was reported by the
261 informants in this study (i.e., disorders caused by the same type of microorganisms). For
262 example, plant species mentioned for treating *tinea pedis* in this study, which included
263 *Cheilocostus speciosus* (J.Koenig) C.D.Specht, *Gmelina arborea*, *Jatropha curcas* L.,
264 *Desmodium velutinum* (Willd.) DC., *Cardiospermum halicacabum* L., *Selaginella willdenowii*,
265 and *Verbena officinalis*, were reported in other studies to be used for treating other fungal
266 infectious disorders such as skin disease, eczema (ringworm), leprous skin, and itches.

267 The 44 distinct uses that were not corroborated in the published literature were all uses
268 shared within an ethnic group. Of those, three uses were uses with high degree of agreement
269 shared between villages (Type 2), i.e., the use of *Toona sinensis* to treat chicken pox by the
270 Hmong (35 citations) including use of *Stephania* sp. (19 citations) and *Pellionia repens* (Lour.)
271 Merr. (10 citations) to treat ringworm by the Mien, while the remaining 41 were plant uses
272 shared within a village of a particular ethnic group (Type 3), including those aforementioned
273 with the highest agreement in use such as the use of *Toona sinensis* to treat dengue by the

274 Hmong (14 citations), and *Dianella ensifolia* to treat cold by the Lua (10 citations)(Appendix 1,
275 ESM).

276 Hence, based on the frequency of citation which reflects the degree of agreement in use
277 of a given plant together with confirmation from other sources, we have determined species
278 which could be additional interesting candidates in the search for new antimicrobial drugs by
279 type of antimicrobial activities as detailed in Appendix 2 (ESM).

280

281 **Discussion**

282

283 The reports of 199 distinct uses of 143 plant species for treating 21 different disorders related to
284 infections by key informants and general informants in this study reflects the large body of
285 traditional knowledge related to infective conditions among the seven ethnic groups that we
286 studied in northern Thailand (Tables 2 and 3). The used species include weeds (e.g., *Bidens*
287 *pilosa* L., *Ageratum conyzoides*, *Eleusine indica*, *Imperata cylindrica* (L.) Raeusch., etc.),
288 introduced species (e.g., *Senna alata* (L.) Roxb., *Mimosa pudica*, *Carica papaya*), as well as
289 widespread species in the tropics (e.g., *Lycopodiella cernua* (L.) Pic. Serm., *Cyperus cyperoides*
290 (L.) Kuntze, *Solanum americanum* Mill.). Because comparing usage between different cultures is
291 an accepted way of highlighting bioactive plants and independent discovery by different ethnic
292 groups provide evidence for bioactivity (Bletter 2007; Heinrich et al. 1998; Johnson 2006;
293 Saslis-Lagoudakis et al. 2011), the agreements we found in 114 distinct uses of 96 species
294 (Appendix 1, ESM) among the informants from the same and different ethnic groups imply that
295 these plants may have therapeutic efficacy for certain kinds of infections. For medicinal uses
296 shared within ethnic groups, the agreement in use may refer to ethnomedicinal knowledge

397 inherited vertically from generation to generation and originating from the ancient ancestors of
398 each ethnic group (Saslis-Lagoudakis et al. 2011). Some ethnomedicinal knowledge may be
399 specific to an ethnic group, representing its intellectual identity, and that situation could be a
300 reason for not being able to corroborate them in the published literature, like the 44 distinct uses
301 presented in Appendix 1 (ESM). In contrast, for plant uses shared between ethnic groups living
302 in the same province (i.e., Nan or Chiang Mai), convergent uses could be considered an
303 indication of efficacy; however, independent discovery cannot be separated from horizontal
304 exchange in this case because horizontal knowledge exchange could occur and lead to common
305 ethnomedicinal use among cultures living in nearby villages and, therefore, shared plant uses
306 may not indicate independent discovery in this case (Saslis-Lagoudakis et al. 2011). The
307 confirmation of plant uses from other distantly located ethnic groups is therefore needed in this
308 context so that the case for independent discovery can be made stronger. In our study, the
309 confirmation of medicinal uses from the literature and ethnobotanical studies, especially those
310 conducted in other distant countries, to all 15 distinct uses shared between ethnic groups lend
311 support to the theory of independently discovered bioactivity of the associated plants, both in
312 case of plant uses shared in the same and in different provinces. Likewise, the confirmations of
313 55 distinct uses shared within ethnic groups (i.e., 11 distinct uses shared between villages and 44
314 shared between informants in the same village) underline the therapeutic efficacy of
315 ethnomedicinal uses passed on from their ancestors.

316 The results from cross-cultural comparison in our study, based on the frequency of
317 citation that reflects the degree of agreement in use of a given plant, together with confirmation
318 from other sources (Appendix 1 and 2, ESM), show that many plants highlighted for possible
319 efficacy in treatment of infections here have been studied pharmacologically and their biological

320 activities have been confirmed. For example, *Gmelina arborea*, *Verbena officinalis*, and *Senna*
321 *alata* have been confirmed for their antifungal activity, *Strobilanthes cusia* (Nees) Kuntze for its
322 antipyretic activity, *Acorus calamus* L. for its antipyretic and antiviral activities, *Combretum*
323 *indicum* (L.) DeFilipps for its anthelmintic activity, *Plumbago zeylanica* L. for its antimalarial
324 activity, *Drynaria quercifolia* (L.) J. Sm. for its antiviral activity, and *Hydrocotyle sibthorpioides*
325 Lam. for its anti-hepatitis virus effect. Some plants have even been developed into new drugs,
326 patented for their medical use, and integrated into the western medicinal practice such as
327 *Lycopodiella cernua* and *Lysimachia christinae* Hance. However, we discovered that the
328 antimicrobial activity related to a particular use of some plants of which uses have been highly
329 agreed among informants and corroborated with uses by distantly located cultures (e.g., use of
330 *Eleusine indica* to treat fever and *Ageratum conyzoides* to treat cold) has not been studied yet.
331 Our study describes ethnomedicinal uses of many species that have not been previously reported
332 for similar use(s) elsewhere, in spite of their wide distributions. Some of those have a high
333 degree of consensus, e.g., *Dianella ensifolia* which was used for treating colds, *Pellionia repens*
334 which was used for treating ringworm, and *Toona sinensis* which was used for treating various
335 infectious disorders including fever, dengue, and chicken pox. These pharmacologically
336 unstudied plants should therefore be placed in high priority in bioscreening for new antimicrobial
337 drugs.

338

339 **Conclusions and perspectives**

340

341 Common patterns of ethnomedicinal uses found within an ethnic group may be attributed to
342 traditional knowledge of the tribe being transmitted vertically from their ancient ancestors,

343 whereas common patterns of ethnomedicinal use found among ethnic groups living near to each
344 other could have resulted from knowledge exchanged horizontally between them, or they could
345 stem from independent discovery of therapeutic efficacy of the plant for ethnic groups with
346 increased distance between them. The convergent uses of some plants reported in our study with
347 those reported in the literature or ethnobotanical studies in distantly located cultures suggest that
348 the bioactivity of a certain plant that may have been discovered independently. Many of the
349 plants highlighted for possible efficacy in treatment of infections here (i.e., plants with high
350 agreement in their uses) have been studied pharmacologically and their biological activities have
351 been confirmed. Some plant uses with high agreement among informants were corroborated with
352 ethnobotanical uses by distantly located cultures but have not been studied for their biological
353 activities, whereas some have been reported in our study for the first time. These
354 pharmacologically unstudied plants should therefore be of interest to pharmacologists and given
355 high priority when bioscreening for new antimicrobial drugs. Considering that the data in this
356 study includes many uses with only a few citations, future research in this field should expand
357 the sampling of both ethnicities and communities to provide more robust evidence. This could be
358 done by coordinating some of the many ethnobotanical activities in Thailand and produce
359 common protocols. As far as making the information available to the community members, they
360 were already briefed about the research when it was ongoing. This work was carried out as part
361 of the program of the ethnobotany group of Chiang Mai University, which is actively engaged in
362 making their research results available to the community, for example through popular books
363 such as that of Trisonthi et al. (2018).

364

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366
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380 **Literature Cited**

381

- 382 Albuquerque, U.P. 2010. Implications of ethnobotanical studies on bioprospecting strategies of
383 new drugs in semi-arid regions. *The Open Complementary Medicine Journal* 2: 21–23.
- 384 Bennett, B.C. and C.E. Husby. 2008. Patterns of medicinal plant use: An examination of the
385 Ecuadorian Shuar medicinal flora using contingency table and binomial analyses. *Journal of*
386 *Ethnopharmacology* 116(3): 422–430.

- 387 Bletter, N. 2007. A quantitative synthesis of the medicinal ethnobotany of the Malinké of Mali
388 and the Asháninka of Peru, with a new theoretical framework. *Journal of Ethnobiology and*
389 *Ethnomedicine* 3: 36. doi: 10.1186/1746-4269-3-36.
- 390 Cook, F.E.M. 1995. *Economic Botany Data Collection Standard*. Royal Botanic Gardens, Kew,
391 London.
- 392 Cowan, M.M. 1999. Plant products as antimicrobial agents. *Clinical Microbiology Reviews*
393 12(4): 564–582.
- 394 Cox, P.A. and M.J. Balick. 1994. The ethnobotanical approach to drug discovery. *Scientific*
395 *American* 270(6): 82–87.
- 396 Dessaint, W. Y. 1981. The Tin (Mal) dry rice cultivators of northern Thailand and northern Laos.
397 *Journal of the Siam Society* 69: 103–137.
- 398 Gilani, A.H. and A.U. Rahman. 2005. Trends in ethnopharmacology. *Journal of*
399 *Ethnopharmacology* 100 (1–2): 43–49.
- 400 Heinrich, M., A. Ankli, B. Frei, C. Weimann, and O. Sticher. 1998. Medicinal plants in Mexico:
401 Healers' consensus and cultural importance. *Social Science and Medicine* 47(11): 1859–1871.
- 402 Hernández, T., M. Canales, J.G. Avila, A. Duran, J. Caballero, A. Romo de Vivar, and R. Lira.
403 2003. Ethnobotany and antibacterial activity of some plants used in traditional medicine of
404 Zapotitlán de las Salinas, Puebla (México). *Journal of Ethnopharmacology* 88: 181–188.
- 405 Hossain, H., P.N. Akbar, S.E. Rahman, T.A. Khan, M.M. Rahman, and I.A. Jahan. 2014. *In vivo*
406 anti-inflammatory and *in vitro* antioxidant activities of *Toona ciliata* leaves native to
407 Bangladesh. *Global Journal of Medical Research* 14(7): 17–26.
- 408 Johnson, L.M. 2006. Gitksan medicinal plants-cultural choice and efficacy. *Journal of*
409 *Ethnobiology and Ethnomedicine* 2: 29. doi: 10.1186/1746-4269-2-29.

- 410 Katiyar, C., A. Gupta, S. Kanjilal, and S. Katiyar. 2012. Drug discovery from plant sources: An
411 integrated approach. *AYU* 33(1): 10–19.
- 412 Martin, G.J. 1995. *Ethnobotany: A methods manual*. London: Chapman & Hall.
- 413 Namita, P. and R. Mukesh. 2012. Medicinal plants used as antimicrobial agent: A review.
414 *International Research Journal of Pharmacy* 3(1): 31–40.
- 415 Nguyen, V.T., T.N. Moong, Q.B. Le, and T.S. Mai. 2009. Research on culture of Khmu people:
416 Case study of Huoi Cang 2 village, Bac Ly commune, Ky Son district, Nghe An province,
417 Vietnam. Hanoi. [http://isee.org.vn/Content/Home/Library/332/research-on-culture-of-khmu-
418 people..pdf](http://isee.org.vn/Content/Home/Library/332/research-on-culture-of-khmu-people..pdf).
- 419 Ong, H.G. and Y.D. Kim. 2014. Quantitative ethnobotanical study of the medicinal plants used
420 by the Ati Negrito indigenous group in Guimaras Island, Philippines. *Journal of
421 Ethnopharmacology* 157: 228–242.
- 422 Perve, E. 2006. *The hilltribes living in Thailand*. Chiang Mai: Alligator Service.
- 423 Pommerville, J.C. 2014. *Fundamentals of microbiology*, 10th ed. Burlington, Massachusetts:
424 Jones & Bartlett Learning.
- 425 Roersch, C.M.F.B. 2010. *Piper umbellatum* L.: A comparative cross-cultural analysis of its
426 medicinal uses and an ethnopharmacological evaluation. *Journal of Ethnopharmacology*
427 131(3): 522–537.
- 428 Saddiqe, Z., A. Maimoona, and S. Khalid. 2013. Phytochemical analysis and anthelmintic
429 activity of extracts of aerial parts of *Solanum nigrum* L. *Biologia (Pakistan)* 59(2): 205–211.
- 430 Saslis-Lagoudakis, C.H., E.M. Williamson, V. Savolainen, and J.A. Hawkins. 2011. Cross-
431 cultural comparison of three medicinal floras and implications for bioprospecting strategies.
432 *Journal of Ethnopharmacology* 135(2): 476–487.

- 433 Schultes, R.E. 1994. Amazonian ethnobotany and the search for new drugs. Ciba Foundation
434 Symposium 185: 106–115.
- 435 Setyawan, A.D. 2009. Traditionally utilization of *Selaginella*; field research and literature review.
436 Nusantara Bioscience 1(3): 146–158.
- 437 Spring, M.A. 1989. Ethnopharmacologic analysis of medicinal plants used by Laotian Hmong
438 refugees in Minnesota. Journal of Ethnopharmacology 26(1): 65–91.
- 439 Tardío, J. and M. Pardo-de-Santayana. 2008. Cultural importance indices: A comparative
440 analysis based on the useful wild plants of southern Cantabria (northern Spain). Economic
441 Botany 62(1): 24–39.
- 442 The Plant List. 2013. Version 1.1. <http://www.theplantlist.org/> (accessed 11.7.17)
- 443 Trisonthi, C., P. Trisonthi, P. Srisanga, and A. Inta. 2018. Ethnobotany: A science of folk
444 wisdom. Chiang Mai: Wanida printing [in Thai].
- 445 Vijayakumar, R., G. Vaijayanthi, A. Panneerselvam, and N. Thajuddin. 2016. Actinobacteria: A
446 predominant source of antimicrobial compounds. Pages 117-142 in D. Dhanasekaran, N.
447 Thajuddin, and A. Panneerselvam, eds. Antimicrobials: Synthetic and natural compounds.
448 Boca Raton, FL: CRC Press.
- 449 Wang, H.K., Y. Xia, Z. Y. Yang, S.L.M. Natschke, and K.H. Lee. 1998. Recent advances in the
450 discovery and development of flavonoids and their analogues as antitumor and anti-HIV
451 agents. Pages 191-226 in J. Manthey and B. Buslig, eds. Flavonoids in the living system.
452 Advances in experimental medicine and biology vol. 439. New York: Springer.
- 453 WHO. 2016. Antimicrobial resistance. <http://www.who.int/mediacentre/factsheets/fs194/en/>
454 (accessed 25.6.17)
- 455 Williams, L.A.D. 2006. Ethnomedicine. West Indian Medical Journal 55(4): 215–216.

456

457 **Table 1** Sixteen villages in northern Thailand where medicinal plants used to treat infections

458 were studied and compared in a cross-cultural context.

459 **Table 2** Frequency of citation and number of medicinal plants used to treat each of the 21

460 categories of infection related disorders [sensu Cook (1995)]. Agreement in use refers to the uses

461 mentioned by at least two informants.

462 **Table 3** Agreement among 103 informants in 16 villages from seven ethnic groups, concerning

463 the use of medicinal plants for the treatment of infections, number of citations, number of

464 combined citations, number of distinct uses, and number of species mentioned for each type of

465 agreement.

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470 **Table 1** Sixteen villages in northern Thailand where medicinal plants used to treat infections were studied and compared in a cross-
 471 cultural context.

Ethnic group	Province	Village	Coordinates	Altitude (masl)	Number of key informants	Number of general informants	Language family
Hmong	Chiang Mai	Khun Mae Wak	18°39'15.68"N, 98°28'28.00"E	1316	1	15	Hmong-Mien
Hmong	Nan	Manee Pruek 1	19°26'22.84"N, 101°04'11.35"E	1252	2	60	Hmong-Mien
Hmong	Nan	Khang Ho	19°07'59.44"N, 100°56'00.38"E	220	2	60	Hmong-Mien
Hmong	Nan	Song Khwae	18°51'49.22"N, 100°38'08.69"E	200	2	60	Hmong-Mien
Khamu	Nan	Huai Pook	18°53'52.81"N, 100°40'53.28"E	220	1	60	Austroasiatic
Khamu	Nan	Huai Satang	19°32'03.64"N,	300	3	60	Austroasiatic

			100°52'13.92"E				
Khamu	Nan	Nam Pan	19°26'14.49"N, 100°40'39.96"E	350	1	60	Austroasiatic
Lahu	Chiang Mai	Pang Kued	19°15'33.05"N, 98°55'17.46"E	900	2	15	Sino-Tibetan
Lisu	Chiang Mai	Khun Jae	19°19'34.54"N, 99°19'13.12"E	1369	1	15	Sino-Tibetan
Lua	Nan	Joon	19°08'40.35"N, 100°55'35.74"E	220	2	60	Austroasiatic
Lua	Nan	Manee Pruek 2	19°24'53.21"N, 101°04'42.18"E	1280	3	60	Austroasiatic
Lua	Nan	Toei Klang	19°13'38.03"N, 101°3'43.70"E	850	1	60	Austroasiatic
Mien	Nan	Huai Labaoya	18°54'31.56"N, 100°40'05.30"E	200	2	60	Hmong-Mien
Mien	Nan	Huai Sanao	19°08'07.19"N,	220	2	60	Hmong-Mien

			100°56'02.79"E				
Mien	Nan	Santiphap	18°59'33.71"N, 100°39'16.50"E	350	1	60	Hmong-Mien
Tai Yuan	Chiang Mai	Mae Kam Pong	18°51'57.94"N, 99°21'7.00"E	1042	2	15	Tai-Kadai

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474 **Table 2** Frequency of citation and number of medicinal plants used to treat each of the 21
 475 categories of infection related disorders [sensu Cook (1995)]. Agreement in use refers to the uses
 476 mentioned by at least two informants.

477

Type of infections	Disorder treated	Questionnaire		Agreement in use	
		# plant species used	Frequency of citation	# plant species used	Frequency of citation
Unspecified	Fever	62	400	37	372
Bacterial	Cholera (in animals; e.g., chicken, horses, pigs)	6	27	3	24
Bacterial	Gonorrhoea	2	7	1	6
Bacterial	Hordeolum	2	10	1	9
Bacterial	Leprosy (in dogs)	3	4	1	2
Bacterial	Meningitis	1	1	1	2
Bacterial	Venereal diseases	3	5	1	3
Fungal	Onychomycosis (<i>Tinea unguium</i>)	1	1	-	-
Fungal	Ringworm (<i>Tinea/Eczema</i>)	21	89	12	80
Fungal	<i>Tinea pedis</i> (Athlete's foot)	20	140	13	133
Helminth worm	Helminth worm infections (e.g., ascariasis, gnathostomiasis, tapeworm)	11	28	5	22

Protozoal	Malaria	5	12	2	9
Viral	AIDS	2	7	1	6
Viral	Chicken pox	9	55	5	51
Viral	Cold	19	79	16	76
Viral	Dengue	1	14	1	14
Viral	Hepatitis	8	20	5	17
Viral	Influenza	3	4	1	2
Viral	Measles	3	8	2	7
Viral	Rabies	1	2	1	2
Viral	Shingles (<i>Herpes zoster</i>)	12	42	6	35
Total		143	955	96	870

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479

480 **Table 3** Agreement among 103 informants in 16 villages from seven ethnic groups, concerning
 481 the use of medicinal plants for the treatment of infections, number of citations, number of
 482 combined citations, number of distinct uses, and number of species mentioned for each type of
 483 agreement.

				484
Type of agreement	Number of citations	Number of combined citations	Number of distinct uses	Number of plant species 485
No agreement	85	85	85	64
Between ethnic groups	331	68	15	12
Within ethnic groups	539	118	99	85
Between village	188	33	14	13
Within village	351	85	85	76
Total	955	271	199	143