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AN ETHNOBOTANICAL META-ANALYSIS OF NORTH AMERICAN MEDICINAL ASTERACEAE

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ABSTRACT

The Asteraceae is the largest family of plants in North America and widely used as medicine by Indigenous peoples. This study investigated the medicinal ethnobotany of North American Asteraceae to identify taxa that appear preferentially selected or avoided for general and specific medicinal uses. Asteraceae-specific ethnobotanical reports recorded in the Native American Ethnobotany Database were compiled and, using residual and binomial analyses, 14 tribes were compared and ranked as either over- or under-selected for medicine, food or technology, and for different categories of medicinal applications. Statistical analysis supported the hypothesis that selection of species for ethnobotanical purposes is non-random and does not depend on the size of the flora. The Anthemideae tribe was identified as over-selected for all types of applications, including most therapeutic categories, most significantly as pulmonary and orthopedic aids. Subsequent analysis revealed that the over-representation of this tribe was attributed mainly to *Achillea millefolium* and *Artemisia spp.*. The significance of Anthemideae, particularly of *Achillea* and *Artemisia* species, as highly-selected medicinal taxa emphasizes their cultural importance to Indigenous North Americans. Residual and binomial statistics generally provided parallel results but supplementary statistical methods, more in-depth investigation of other use categories, and inclusion of plant distribution data may provide greater insight into traditional uses of Asteraceae in North America.

KEYWORDS:

Ethnobotany; herbal medicine; Compositae; plant diversity; Anthemideae; *Achillea millefolium*; *Artemisia*

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INTRODUCTION

The Asteraceae (Compositae) is the largest family of flowering plants in North America. In addition to its diversity, the Asteraceae is also the most medicinally used family among Indigenous Peoples across the continent. Studies investigating patterns of medicinal plant selection worldwide show significant similarities in both over-selected and under-selected taxa by communities in different regions across the globe (Moerman et al., 1999; Saslis-Lagoudakis et al., 2011). As the first ethnobotanical meta-analysis of its kind, a combination of regression and residual analyses (Moerman, 1991) was used to evaluate potential relationships between the size of a plant family and the number of species within that family selected for medicinal use. If this relationship is random, it is expected that, as the size of a family increases, the number of medicinal species within that family will increase proportionately. Supporting the hypothesis that selection *is not random,* certain families were found to contain more or fewer medicinal species than expected based on family size (i.e. the number of species in North America as reported by Shetler and Skog (1978)). These data were ranked by their corresponding residual values, where a large positive or negative residual respectively represented a family favoured or avoided/ignored for medicinal use. Moerman (1991) compared 14 taxa at the family level and concluded that the Asteraceae family contains the largest number of medicinally used species and are more highly selected than expected. This result was consistent across cultures from well-separated geographical regions (Moerman et al., 1999; Leonti et al., 2003; Morales & Ladio, 2009; Saslis-Lagoudakis et al., 2011; Plumthum et al., 2019).

Motivated by the ethnobotanical significance of this plant family, the current study evaluated the medicinal applications of North American Asteraceae, specifically, and assessed their prevalence of use in traditional practices. Because regression and residual analytical methods bias large families, this review also applied binomial analysis to gauge over- and under-selection of medicinal Asteraceae taxa by Indigenous Peoples of North America. Like residual analysis, the binomial method hypothesizes that the proportion of medicinal species in the total flora is the same as the proportion of medicinal species

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within a family. Statistically significant deviation from this proportion for any given family thereby indicates over- or under-selection for medicinal use. Ranking according to probability rather than residuals, binomial analysis does not bias based on the family size (Bennett & Husby, 2008).

Using the online Native American Ethnobotany (NAEB) database, this study compiled a list of Asteraceae species and their ethnobotanical uses to identify tribes, genera or species that are over-utilized as medicinal aids. It was hypothesized that the selection of North American Asteraceae species, based on reported use by Indigenous Peoples, is non-random and taxa are actively favoured or avoided for use as medicinal aids across different therapeutic categories. Phylogenetic and geographical analyses of ethnobotanically significant taxa were also discussed.

METHODS

Collection and Organization of Ethnobotanical Data

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Reports of ethnobotanical North American Asteraceae species were collated and reviewed using the online Native American Ethnobotany (NAEB) database (Moerman, 2003). This database summarizes published reports of traditional plant uses by ~300 Indigenous "tribes" across North America into the following use categories: drug, food, fiber, dye, and other. Note that, in this study, the term "tribe" as defined in the NAEB database was replaced with the Canadian terms "Indigenous Peoples" or "(First) Nations". The NAEB database contains over 44,000 entries dating back >100 years and relating to 243 different plant families. Each database entry provides a concise report of a particular species, its use category, the part(s) of the plant used and how it is administered, as well as the Indigenous community from which the account was reported/observed. Medicinal reports are further organized into ten categories based on their reported therapeutic use (Supplementary Data). All North American Asteraceae taxa were identified based on the Flora of North America (2006), which consists of 2413 species belonging to 418 genera. The NAEB database was then queried with each genus name. All reports were collected and organized by appropriate taxa, creating a complete dataset of ethnobotanical Asteraceae.

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When ethnobotanical reports referenced specific sub-species or varieties, data were collected for this sub-species or variety as a separate taxon within the genus, and reports referencing a genus non-specifically were pooled into a single taxon (e.g. *Aster sp.*) for meta-analytical purposes. Each entry was grouped into one of three categories: medicine ('drug'), technology ('fibre' and 'dye'), or food. Medicinal uses were then coded according to medicinal category, plant part used, and associated Indigenous nation.

Phylogenetic Organization of Taxa

Organization of Asteraceae taxa into tribes and subtribes followed the Flora of North America (2006) but the phylogenetic groupings of the most prominent ethnobotanical genera and species were cross-referenced with more recent genomic data (Oberprieler, Himmelreich, & Vogt, 2007) to provide a more accurate representation of known systematic relationships.

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Residual Analysis

All residual analyses were performed in RStudio (Version 1.0.153) based on methods used by Moerman (1991; 1996; et al., 1999). Asteraceae taxa were assessed in terms of their likelihood to be over- or under-used as a medicinal aid. Variables were compared using least squares linear regression analysis using the lm() function and the 'dplyr' R package. Residual values were calculated in order to compare results across the Asteraceae family, by subtracting the observed value from the expected value attained from the linear regression.

Binomial Analysis

All binomial analyses were performed in Excel based on methods used by Bennett and Husby (2008) and Turi and Murch (2013). For each analysis, the null hypothesis was that the proportion of uses or species selected as ethnobotanical aids was equal to the total number of uses or species. The

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alternative hypotheses stated that this proportion was either greater or less than the total proportion within the flora. Analyses were carried out using the BINOM.DIST function in Excel.

RESULTS

META-ANALYSIS OF ETHNOBOTANICAL REPORTS FOR MEDICINAL, DIETARY AND TECHNOLOGICAL PURPOSES

Initially, a general analysis of reported ethnobotanical uses of Asteraceae by North American Indigenous nations was completed, evaluating the total number of species within each tribe relative to the number of species used for medicine, food, or technology. Residual and binomial analyses provided similar results, generally identifying the same tribes as most over- and under-selected for each of the three use categories, but often with different ranking (Table 1). The Anthemideae was the most over-selected Asteraceae tribe for medicinal (Figure 1A) and technological applications and, based on binomial analysis, the only tribe for which selection reached significance. The Anthemideae was also among the most favoured tribes for dietary use, securing its position as the family's most ethnobotanically-selected tribe in North America (Table 1). The Cardueae, Cichorieae and Heliantheae were also significantly over-represented as food plants, with the Cichorieae and Cardueae ranking second and third based on all ethnobotanical uses. Contrary to the Anthemideae, the Eupatorieae was the most under-utilized tribe across all purposes, including medicine and technology, and was significantly under-selected for food. The Senecioneae was significantly under-represented as medicines and the Astereae was the most under-selected tribe for food (Table 1).

Comparison of *total number of use reports* (rather than number of species used) versus total available species across tribes offered the most pronounced illustration of a selection bias toward Anthemideae among North American Indigenous peoples. Whereas the Anthemideae (99 species) ranks 8th of 14 North American Asteraceae tribes in terms of species richness, it was the most ethnobotanically

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cited tribe, with more reported uses for medicine (Figure 1B) or technological purposes (Supplemental data) than any other tribe, including the Astereae and Heliantheae (>700 species each).

Note that, by this metric, nearly all other tribes are under-utilized as medicine with the Anthemideae as the clear outlier. Arguments for successful binomial analyses require the probability of success on each trial to be between 0 and 1, and that number of successes ≤ number of independent trials. These arguments were not met since use counts (number of successes) were always higher than number of species (number of trials) so no statistical analyses were completed for this data set.

META-ANALYSIS OF MEDICINAL ASTERACEAE

Subsequent analyses focused only on medicinal applications, since medicinal uses accounted for >75% of all ethnobotanical reports for the family. To explore whether different Asteraceae taxa appear selectively used for specific medicinal purposes, residual and binomial analyses were repeated for each of ten medicinal use categories to again identify over- and under-selected tribes within each category.

We initially compared the number of species in a tribe selected for each of the ten medicinal use categories relative to the total species number in North America, revealing that, across all categories, Anthemideae was the top ranked, most over-represented tribe based on residual and binomial analyses (data not shown). Because species of this tribe were so highly selected compared to species richness (Figure 1), the analyses were repeated using the number of species used for each medicinal category compared to the total number of *medicinal species* in each tribe. Again, across all categories, Anthemideae was the most over-represented tribe based on residual data (Table 2), with binomial analysis yielding almost identical results; the Anthemideae was significantly over-used in all medicinal categories except cardiology, for which only the Vernonieae appeared preferentially selected (Table 2). The Plucheeae (neurological) and Eupatorieae (orthopedic) were the only other over-selected tribes across medicinal use categories. In contrast, whereas residual analysis suggested that Astereae species were consistently under-utilized by North American Indigenous peoples in most therapeutic categories,

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binomial tests revealed that these trends were only significant for the dermatological, orthopaedic, and general categories (Table 2). Cichorieae species were strongly under-represented among taxa used as pulmonary or gastrointestinal aids.

The most significant category for which Anthemideae species were over-utilized was pulmonary, which yielded the highest residual value (15.77), and lowest *P*-value (1×10^{-06}) (Table 2, Figure 2A). However, as the most cited tribe in nine out of ten medicinal categories, the Anthemideae may simply be favoured as medicine, in general. Despite accounting for only 4.1% of North American Asteraceae species, the Anthemideae represent 15-42% of Asteraceae use reports across all medicinal categories (Figure 2). To differentiate between taxa that are generally over-selected as a medicine from those that are actively selected for more specific therapeutic purposes, we investigated a second level of selection – the number of use counts within each of the ten medicinal categories relative to the total number of medicinal use reports for each Asteraceae tribe (Supplementary data). Here, the null hypothesis was that the use of a taxon for one medicinal purpose or another is random, and that the proportion of specific medicinal uses relative to total medicinal uses is consistent across taxa (i.e. as the total medicinal uses within a tribe increases, the number of any specific medicinal use will increase proportionately). This comparison suggested that selection for specific purposes in not random and that the Anthemideae – relative to their total medicinal uses – were significantly over-selected as pulmonary ($p = 0.0001$, Figure 2B) and orthopedic ($p = 0.007$) aids but *under-selected* for uses related to cardiological ($p = 0.006$) and gynecological ($p = 0.012$) conditions (Supplemental data). Compared to the consistent positive bias seen through our initial standard analyses, these findings suggest that Anthemideae species are highly selected for use across all treatment categories (relative to other taxa) but specifically over-selected for pulmonary and orthopedic applications (relative to other medicinal uses) (Figure 3).

A closer look at pulmonary reports identified the Anthemideae as the most frequently cited tribe for use as a cold remedy, cough medicine, pulmonary aid and respiratory aid, with the Astereae accounting for 4 of only 6 reported uses as an expectorant (Table 3).

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Analysis of Medicinal Anthemideae

The significance of Anthemideae species as preferred treatments for diverse medicinal purposes prompted further assessment. The Anthemideae tribe consists of 110 genera distributed predominantly throughout the Mediterranean, southern Africa, and central Asia; however, there is also an abundance of North American species. Fourteen subtribes are recognized globally but only three closely related subtribes occur in North America: Anthemidinae, Matricariinae, and Artemisiinae, the largest group (Oberprieler, Himmelreich, & Vogt, 2007; Watson et al., 2002). Sample size (number of sub-tribes, genera and taxa per genus) was insufficient for statistical analysis, a comparison of medicinal species and use reports across treatment categories revealed that, relative to medicinal taxa within genera, *Achillea spp*. were most frequently cited (364 reports, 355 for *A. millefolium* and recognized North American varieties), followed by *Artemisia spp.* (≈24 use reports per taxon) (Table 4).

Focusing specifically on the most highly over-selected treatment categories, the number of reports of pulmonary and orthopedic uses per taxon was presented relative to the phylogenetic relationships of medicinal Anthemideae (Figure 4) following revised classifications based on molecular data (Oberprieler, Himmelreich, & Vogt, 2007; Torrell et al., 1999; Watson, Evans, & Boluarte, 2000; Watson et al., 2002). *Artemisia tridentata* Nutt. (44 reports) and *Achillea millefolium* L. (30 reports) were most cited as pulmonary aids, more than twice as many times of as any other species (Figure 4A). *Achillea millefolium* (19 reports) was the most cited for orthopedic uses, followed by three *Artemisia* species, *A. dracunculus, A. tridentata, A. douglasiana* (with 14, 13, and 12 reports, respectively) (Figure 4B).

DISCUSSION

Since ethnobotanical meta-analyses have consistently identified the Asteraceae as one of the most highly selected families for medicinal purposes, in North America and around the world (Moerman et al.,

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1999; Leonti et al., 2003; Molares & Ladio, 2009; Saslis-Lagoudakis et al., 2011; Plumthum et al., 2019), this meta-analysis focused solely on Asteraceae ethnobotany among Indigenous peoples of North America. Our study confirmed the hypothesis of non-random selection of taxa for different purposes, including medicine, diet, and technology. Whereas the Eupatorieae tribe was most significantly under-represented based on comparison of medicinal species relative to total species (Table 1), the Anthemideae was the most over-selected for nearly all uses, notably 9/10 medicinal use categories (Tables 1-2). The strong bias toward this tribe for medicinal and technological applications obscured the relative significance of other tribes for such purposes. The apparent aversion to Eupatorieae, and to a lesser degree Senecioneae, may reflect the prevalence of toxic pyrrolizidine alkaloids and sesquiterpenes produced by these taxa (Liu et al., 2015; Schrenk et al., 2020). In contrast, over-selection of Cardueae, Cichorieae and Heliantheae for food was based, respectively on the widespread consumption of edible *Cirsium* (e.g. thistle), *Taraxacum* (dandelion) and *Lactuca* (lettuce), and *Helianthus* (sunflower) and *Balsamorhiza* (balsamroot) species (Turner et al., 2011; Turner, 2020).

Due to the overwhelming over-representation of Anthemideae for medicinal uses, secondary analyses focused on these data, highlighting the prolific use of *Achillea millefolium* L. (yarrow) and *Artemisia spp.* (sagebrush) for treating all medicinal categories, and for nearly all pulmonary and orthopedic uses (Figure 4, Table 4). Notably, the global ethnomedical significance of both taxa are well-documented (Wright, 2001; Applequist & Moerman, 2011; Turner, 2018) and, when data for these genera are excluded from our analyses, the Anthemideae is no longer an over-represented tribe in terms of either medicinal species or use reports (Figure 1, Table 4). Turi and Murch (2013) also identified *Artemisia* as the most over-utilized of all North American genera as ceremonial and spiritual plants. Indeed, ceremonial use reports of *Artemisia spp.* represented nearly 25% and 10% of total technological uses among Anthemideae and Asteraceae, respectively, driving the selection observed in the current meta-analysis (data not shown). The therapeutic potential of both genera are also supported by pre-

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clinical studies characterizing their bioactivity and associated phytochemicals (Bora & Sharma, 2011; Ali et al., 2017; Kachura et al., 2018).

The three main classes of phytochemicals within Anthemideae are flavonoids, polyacetylenes, and terpenes (Greger, 1977), with other classes and overall metabolic profile varying between taxa. Relevant to pulmonary uses, luteolin, a flavonoid found in yarrow and sagebrush (Lopez-Lazaro, 2009; Gudzenko, 2013), contributes to the bronchodilatory effects of *Artemisia afra* in isolated perfused lungs (Mjiqiza et al., 2013). Both yarrow and sagebrush species also possess antibiotic activities (Maz, Mirdeilami, & Pessarakli, 2013; Sarker, Nahar, & Kumarasamy, 2007; Lopez-Lutz et al., 2008; Obistioiu et al., 2014) that may help protect against infections of the lungs (or other organs), and immunomodulatory effects that may help with symptoms of, and recovery from, infection – as well as rheumatism. Three of the four most cited species for orthopedic uses (yarrow, *Artemisia dracunculus* (tarragon) and *A. douglasiana*) have reported anti-inflammatory activity in animal models (Goldberg et al., 1969; Guardia et al., 2003; Molina-Hernandez et al., 2004; Eidi et al., 2016). Interestingly, both yarrow and tarragon produce alkylamides (Saadali et al., 2001; Veryser et al., 2017), which contribute to the anti-inflammatory and nociceptive properties of *Echinacea spp.* (Heliantheae) (Olah et al., 2017; Rui et al., 2021). Few studies, however, have investigated the therapeutic potential of *A. tridentata*, which had more than twice as many medicinal use reports than any other sagebrush species. Given the ethnobotanical and ecological significance of the Tridentatae subgenus, which is endemic to North America, more pharmacological and phytochemical research on these species is warranted (Turi et al., 2014).

Beyond bioactivity, the pervasive use of yarrow and sagebrush in North America for similar medicinal applications, including coughs and colds, serves as an example of medicinal plant knowledge exchange (Turner, 2018). Species distribution also impacts access to, and sharing of, medicinal knowledge and resources, with use of widely distributed medicinal plants more easily transferred between First Nations. While the continental distribution of yarrow and *A. ludoviciana ssp. ludoviciana*

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likely contribute to their high ethnobotanical use counts, *A. tridentata* is found predominantly in the western United States, where it has been identified as one of the region's most culturally significant plants (Stoffle et al., 1990). Studies employing phylogenetic methods with the goal of discovering medicinal plants report that bioactivity and medicinal properties are not randomly distributed in plant phylogenies, noting that closely related species are selected for similar ethnobotanical uses (Lukhoba, Simmonds, & Paton, 2006; Saslis-Lagoudakis et al., 2011). The presence and abundance of phytochemicals in medicinally relevant species could also aid in identification. For example, many *Artemisia* species contain high levels of volatile sesquiterpene lactones with aromatic properties (Goff & Klee, 2006; Turi, Shipley, & Murch, 2014), making them distinguishable as related species and possibly selected for similar purposes. Given the broad geographical distribution and abundance of many Asteraceae taxa, as well as botanical and organoleptic similarities among related species, these phenomena may contribute to the high proportion of medicinal species and uses of Asteraceae, more generally.

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Comparing the distribution of First Nations communities with the geographical distribution of pulmonary Anthemideae species demonstrates that this relationship is not always congruent. Pulmonary medicinal uses recorded within Shoshoni, Paiute, and Thompson - three First Nations groups located in western North America - account for 30% of the total pulmonary uses for all species. When comparing distributions of Shoshoni and Paiute with top ranking Artemisia species, it is notable that the selection of these medicinal species is not random and does not solely depend on geographical distribution and accessibility of the species. Shoshoni are more likely select widely distributed *Artemisia* species over those found only in their geographical location. This could indicate that traditional knowledge of the selected species as a pulmonary aid is well established so selected over other species. It is noteworthy that various cultures, communities, and indigenous groups across the northern hemisphere are known to use certain Asteraceae species for similar medicinal applications (Moerman et al., 1999). Whereas intercultural knowledge transfer remains likely, the common uses of these species by geographically

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distinct cultural groups suggests that similar knowledge of medicinal plants has been generated independently by these separate groups.

The limitations of meta-analytical approaches to hypothesis testing in ethnobotany have been well discussed (Weckerle et al., 2012; Turi & Murch, 2013; Leonti et al., 2020) and deserve consideration. Whereas this review can be described as secondary ethnobotany, data on which our analyses were based was generated through primary ethnobotany studies that documented human relationships with plants using different methods and under different contexts. Accuracy and consistency in the translation of primary sources, often obtained through verbal and inter-cultural exchanges, into codified (and often overlapping) medical terms and categories is therefore complicated. The "ethnobotanical coverage" across North America is also unequal, leading to disproportional representation of some Nations and regional flora within the NAEB database. Finally, the statistical methods to identify over- and under-selected taxa were not exhaustive but, given the significance observed for Anthemideae, *Achillea* and *Artemisia* using binomial analysis, we did not pursue additional techniques.

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CONCLUSIONS

Using the NAEB database and multivariate analyses, the medicinal significance of Asteraceae tribes used by Indigenous peoples in North America was assessed. Although the applied residual and binomial analyses could be complemented by additional hypotheses and statistical approaches, the significance of Anthemideae species – particularly yarrow and sagebrush – as highly selected medicinal plants for most therapeutic uses, notably as pulmonary and orthopedic aids, was unambiguous. With few North American species, *Achillea* (mainly *A. millefolium*) has received significant research attention to date but with limited focus on pulmonary/respiratory and orthopedic outcomes. Despite their ethnobotanical prominence and greater biodiversity, North American *Artemisia* species remain poorly studied and warrant further investigation.

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Table 1 – Most over- and under-selected Asteraceae tribes for ethnobotanical use (medicine, food, technology, all purposes) based on residual and binomial analyses Data analysis compared total number of medicinal, technological, and food species to total number of species in each tribe. For over-selection, tribes are listed in order of highest (positive) residual value and greatest significance (lowest p-value, binomial analysis). For under-selection, tribes are listed in order of lowest (negative) residual value and greatest significance (lowest *p*-value, binomial analysis). Tribes that were significantly over- or under-represented (p-value < 0.05) are in bold font.

	Over-selected tribes				**Under-selected tribes**			
Rank	**Residual**		**Binomial (*p*-value)**		**Residual**		**Binomial (*p*-value)**	
MEDICINAL					***MEDICINAL***			
1	Anthemideae	24.36	**Anthemideae**	**$1.5e^{-08}$**	Eupatorieae	-12.1	**Eupatorieae**	**0.008**
2	Astereae	5.97	Plucheeae	0.193	Senecioneae	-9.62	**Senecioneae**	**0.034**
3	Cichorieae	5.54	Cichorieae	0.210	Heliantheae	-5.18	Calenduleae	0.219
4	Plucheeae	0.97	Mutisieae	0.285	Gnaphalieae	-2.93	Heliantheae	0.257
5	Mutisieae	0.60	Astereae	0.380	Calenduleae	-2.07	Gnaphalieae	0.308
DIETARY					***DIETARY***			
1	Heliantheae	24.9	**Cardueae**	**$1.2e^{-4}$**	Astereae	-30.2	**Astereae**	**$3.0e^{-08}$**
2	Cichorieae	16.2	**Cichorieae**	**$3.7e^{-4}$**	Eupatorieae	-7.85	**Eupatorieae**	**0.010**
3	Cardueae	12.2	**Anthemideae**	**0.002**	Gnaphalieae	-5.48	Gnaphalieae	*0.052*
4	Anthemideae	8.36	**Heliantheae**	**0.007**	Senecioneae	-5.42	Senecioneae	0.076
TECHNOLOGICAL					***TECHNOLOGICAL***			
1	Anthemideae	21.1	**Anthemideae**	**$1.9e^{-11}$**	Eupatorieae	-5.55	Eupatorieae	*0.052*
2	Astereae	5.23	Astereae	0.317	Cichorieae	-4.83	Gnaphalieae	0.067
3	Cardueae	0.08	Cardueae	0.478	Gnaphalieae	-4.62	Cichorieae	0.120
4					Heliantheae	-4.42	Heliantheae	0.198
ALL PURPOSES								
1	Anthemideae	26.9	**Anthemideae**	**$6.9e^{-9}$**	Eupatorieae	-21.0	**Eupatorieae**	**$5.1e^{-5}$**
2	Cichorieae	19.4	**Cichorieae**	**0.003**	Senecioneae	-14.1	**Senecioneae**	**0.007**
3	Cardueae	8.36	**Cardueae**	**0.047**	Gnaphalieae	-7.32	Gnaphalieae	0.080
4	Astereae	1.69	Plucheeae	0.414	Vernonieae	-3.54	Calenduleae	0.110

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Table 2 - Residual and binomial analysis of the number species in a tribe selected for each medicinal category, relative to the total number of medicinal species in the tribe.

Over-selected tribes

	CAR		**DER**		**GEN**		**GIM**		**GYN**	
Residual		Residual		Residual		Residual		Residual		Residual
1	Anthemideae	2.13	Anthemideae	12.85	Anthemideae	5.70	Anthemideae	7.46	Anthemideae	8.14
2	Vernonieae	1.21	Heliantheae	4.12	Heliantheae	3.48	Heliantheae	6.95	Heliantheae	2.61
3	Heliantheae	0.90	Senecioneae	2.83	Eupatorieae	1.63	Eupatorieae	3.77	Cardueae	0.61
4	Cardueae	0.90	Cardueae	2.59	Cardueae	1.47	Cardueae	1.86	Eupatorieae	0.26
Binomial		*p*-value		*p*-value		*p*-value		*p*-value		*p*-value
1	**Vernonieae**	**0.044**	**Anthemideae**	**0.0001**	**Anthemideae**	**0.013**	**Anthemideae**	**0.020**	**Anthemideae**	**0.010**
2	Inuleae	0.091	Senecioneae	0.121	Inuleae	0.104	Eupatorieae	0.051	Inuleae	0.341
3	Anthemideae	0.210	Cardueae	0.123	Eupatorieae	0.128	Heliantheae	0.224	Mutisieae	0.422
4	Cardueae	0.30	Inuleae	0.422	Cardueae	0.168	Cardueae	0.242	Vernonieae	0.422

	NEU		**ORT**		**OTH**		**OTO**		**PUL**	
Residual										
1	Anthemideae	10.34	Anthemideae	10.62	Anthemideae	8.89	Anthemideae	10.65	Anthemideae	15.77
2	Plucheeae	2.41	Eupatorieae	4.15	Senecioneae	1.56	Cardueae	1.98	Gnaphalieae	2.50
3	Inuleae	0.61	Heliantheae	2.58	Eupatorieae	0.78	Vernonieae	0.67	Eupatorieae	1.50
4	Vernonieae	0.41	Senecioneae	0.43	Cardueae	0.67	Astereae	0.09	Heliantheae	1.20
Binomial										
1	**Anthemideae**	**0.001**	**Anthemideae**	**0.0006**	**Anthemideae**	**0.005**	**Anthemideae**	**0.0007**	**Anthemideae**	**1.1E-06**
2	**Plucheeae**	**0.025**	**Eupatorieae**	**0.0138**	Senecioneae	0.300	Cardueae	0.219	Gnaphalieae	0.100
3	Inuleae	0.401	Inuleae	0.223	Eupatorieae	0.401	Vernonieae	0.317	Eupatorieae	0.213
4	Eupatorieae	0.517	Senecioneae	0.408	Cardueae	0.432			Inuleae	0.263

Under-selected tribes

	CAR		**DER**		**GEN**		**GIM**		**GYN**	
Residual		*Residual*		*Residual*		*Residual*		*Residual*		*Residual*
1	Astereae	-1.56	Astereae	-7.16	Astereae	-4.98	Astereae	-6.77	Astereae	-4.34
2	Senecioneae	-1.25	Gnaphalieae	-3.65	Plucheeae	-1.22	Cichorieae	-6.25	Gnaphalieae	-3.74
3	Gnaphalieae	-0.95	Cichorieae	-2.43	Vernonieae	-1.22	Gnaphalieae	-3.23	Senecioneae	-2.04
4	Mutisieae	-0.79	Plucheeae	-1.95	Mutisieae	-1.22	Senecioneae	-2.04	Plucheeae	-0.87
Binomial		*p-value*		*p-value*		*p-value*		*p-value*		*p-value*
1	Astereae	0.227	**Astereae**	**0.027**	**Astereae**	**0.014**	**Cichorieae**	**0.042**	Gnaphalieae	0.068
2	Senecioneae	0.366	Gnaphalieae	0.119	Cichorieae	0.397	Astereae	0.081	Astereae	0.157
3	Gnaphalieae	0.472	Cichorieae	0.227	Senecioneae	0.566	Gnaphalieae	0.130	Senecioneae	0.280
4	Heliantheae	0.506	Plucheeae	0.437	Mutisieae	0.644	Senecioneae	0.289	Cichorieae	0.555

	NEU		**ORT**		**OTH**		**OTO**		**PUL**	
Residual		*Residual*		*Residual*		*Residual*		*Residual*		*Residual*
1	Astereae	-1.56	Astereae	-7.16	Astereae	-4.98	Astereae	-6.77	Astereae	-4.34
2	Senecioneae	-1.25	Gnaphalieae	-3.65	Plucheeae	-1.22	Cichorieae	-6.25	Gnaphalieae	-3.74
3	Gnaphalieae	-0.95	Cichorieae	-2.43	Vernonieae	-1.22	Gnaphalieae	-3.23	Senecioneae	-2.04
4	Mutisieae	-0.79	Plucheeae	-1.95	Mutisieae	-1.22	Senecioneae	-2.04	Plucheeae	-0.87
Binomial		*p-value*		*p-value*		*p-value*		*p-value*		*p-value*
1	Cichorieae	0.052	**Astereae**	**0.039**	**Vernonieae**	**0.033**	Eupatorieae	0.064	**Cichorieae**	**0.001**
2	Senecioneae	0.121	Cichorieae	0.050	Mutisieae	0.209	Senecioneae	0.076	Astereae	0.111
3	Mutisieae	0.129	Vernonieae	0.365	Heliantheae	0.250	Mutisieae	0.265	Mutisieae	0.295
4	Gnaphalieae	0.160	Heliantheae	0.405	Gnaphalieae	0.252	Heliantheae	0.324	Vernonieae	0.295

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Table 3 - Use counts of North American Asteraceae tribes selected for pulmonary and orthopedic uses. Number of uses collected from NAEB Database (Moerman, 1991; 2003; 2009).

Tribe	Pulmonary (PUL) uses				Orthopedic (ORT) uses		
	Cold Remedy	Cough Medicine	Expectorant	Pulmonary Aid	Orthopedic aid	Antirheumatic - external	Antirheumatic - internal
Anthemideae	98	32	1	15	33	57	7
Astereae	33	26	4	10	17	8	0
Cardueae	1	1	1	3	1	8	4
Cichorieae	2	1	0	2	6	1	0
Eupatorieae	10	2	1	1	2	8	4
Gnaphalieae	14	7	0	2	4	3	2
Heliantheae	21	11	0	9	19	18	11
Inuleae	4	2	0	4	0	1	0
Plucheeae	1	0	0	1	1	0	0
Senecioneae	6	7	0	3	4	4	1

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Table 4 - Use counts of North American Anthemideae genera selected for ten medicinal use categories. Number of uses collected from NAEB Database (Moerman, 1991; 2003; 2009).

Genus	# Medicinal taxa	# Medicinal reports	# Use Reports									
			CAR	DER	GEN	GIM	GYN	NEU	ORT	OTH	OTO	PUL
Achillea	6	364	6	62	8	58	27	54	23	51	36	39
Artemisia	29	698	2	75	8	93	55	81	66	168	39	111
Tanacetum	2	39	0	2	1	10	6	6	4	7	2	1
Picrothamnus	1	18	0	7	0	1	2	1	1	1	0	5
Leucanthemum	1	7	0	1	0	0	0	1	0	4	1	0
Chamaemelum	1	7	0	1	0	3	1	1	0	1	0	0
Matricaria	2	46	1	2	3	15	3	5	0	13	0	4
Anthemis	2	37	1	1	1	9	4	8	2	6	2	3

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FIGURE CAPTIONS

Figure 1 – Scatter plot of A) medicinal species relative to total species, and B) number of medicinal use reports relative to total species for 14 North American Asteraceae tribes. Linear regressions follows the equations (A) y = 0.1909x + 0.7314, R2 = 0.9685, and (B) y = 1.0238x + 97.253, R2 = 0.42371. Ant-Anthemidae, Arc-Arctotideae, Ast-Astereae, Cal-Calenduleae, Car-Cardueae, Cic-Cichorieae, Eup-Eupatorieae, Gna-Gnaphalieae, Hel-Heliantheae, Inu-Inuleae, Mut-Mutisieae, Plu-Plucheeae, Sen-Senecioneae, Ver-Vernonieae

Figure 2 – Linear regression plots of 14 North American Asteraceae tribes illustrating selection bias toward Anthemideae as pulmonary aids. Plots compare A) total number of medicinal species and number of pulmonary medicinal species per tribe (regression follows the equation y = 0.2294x + 1.1397, $R^2 = 0.8152$) and, B) total number of medicinal uses with number of pulmonary uses per tribe (regression follows the equation y = 0.1076x – 1.9514, $R^2 = 0.8485$). Ant-Anthemidae, Arc-Arctotideae, Ast-Astereae, Cal-Calenduleae, Car-Cardueae, Cic-Cichorieae, Eup-Eupatorieae, Gna-Gnaphalieae, Hel-Heliantheae, Inu-Inuleae, Mut-Mutisieae, Plu-Plucheeae, Sen-Senecioneae, Ver-Vernonieae

Figure 3 - Number of medicinal use reports by therapeutic category among Anthemideae species (black bars) and all Asteraceae species (complete bars). The percentage of Asteraceae use reports attributed to Anthemideae species is indicated above each category. Ten medicinal therapeutic categories are listed as in Moerman (1991) and defined in Supplemental Data.

Figure 4 – Medicinal use reports of Anthemideae for pulmonary (A) and orthopedic (B) purposes relative to the phylogenetic relationship among three North American subtribes and their medicinal taxa. Tree construction based on phylogenetic subtribal classification data (Oberprieler, Himmelreich, & Vogt, 2007; Torrell et al., 1999; Watson, Evans, & Boluarte, 2000; Watson et al., 2002). Number of medicinal use reports correspond with final branch size.

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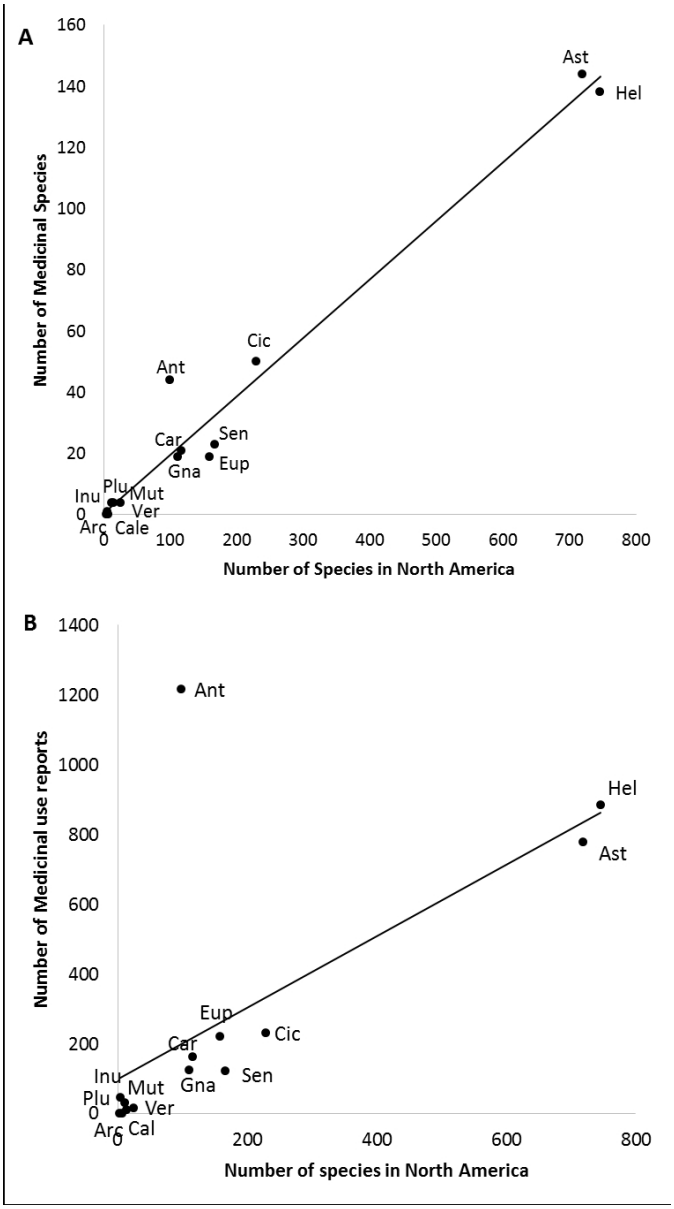


Figure 1 – Scatter plot of A) medicinal species relative to total species, and B) number of medicinal use reports relative to total species for 14 North American Asteraceae tribes. Linear regressions follows the equations (A) y = 0.1909x + 0.7314, R2 = 0.9685, and (B) y = 1.0238x + 97.253, R2 = 0.42371. Ant-Anthemidae, Arc-Arctotideae, Ast-Astereae, Cal-Calenduleae, Car-Cardueae, Cic-Cichorieae, Eup-Eupatorieae, Gna-Gnaphalieae, Hel-Heliantheae, Inu-Inuleae, Mut-Mutisieae, Plu-Plucheeae, Sen-Senecioneae, Ver-Vernonieae

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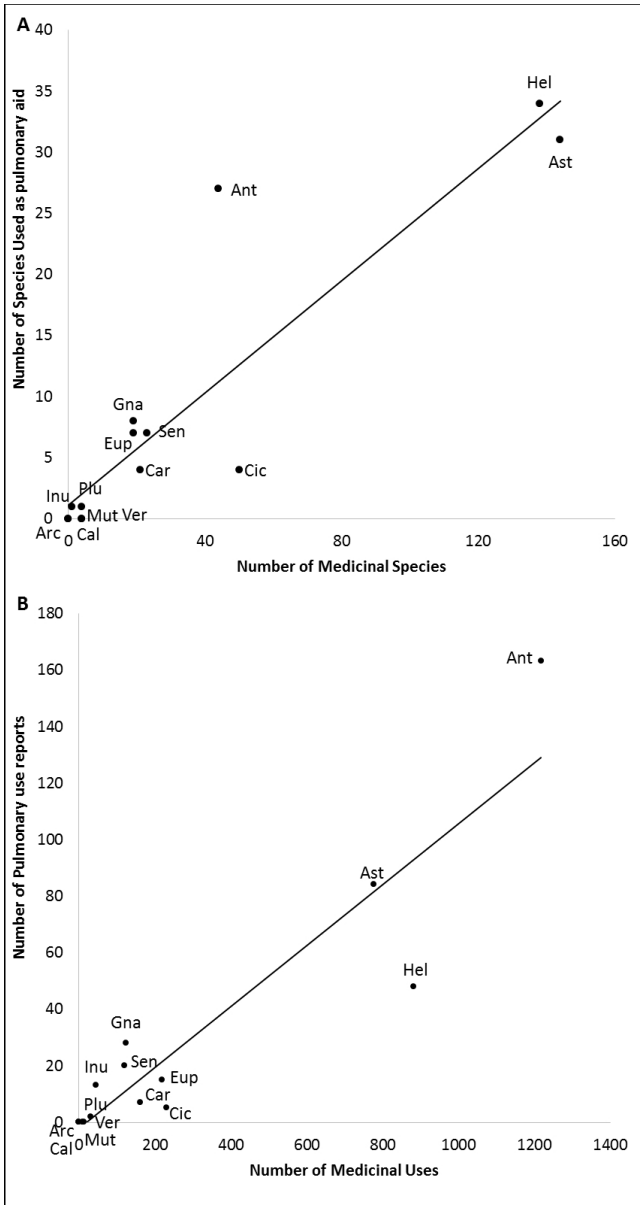


Figure 2 – Linear regression plots of 14 North American Asteraceae tribes illustrating selection bias toward Anthemideae as pulmonary aids. Plots compare A) total number of medicinal species and number of pulmonary medicinal species per tribe (regression follows the equation y = 0.2294x + 1.1397, R2 = 0.8152) and, B) total number of medicinal uses with number of pulmonary uses per tribe (regression follows the equation y = 0.1076x – 1.9514, R2 = 0.8485). Ant-Anthemidae, Arc-Arctotideae, Ast-Astereae, Cal-Calenduleae, Car-Cardueae, Cic-Cichorieae, Eup-Eupatorieae, Gna-Gnaphalieae, Hel-Heliantheae, Inu-Inuleae, Mut-Mutisieae, Plu-Plucheeae, Sen-Senecioneae, Ver-Vernonieae

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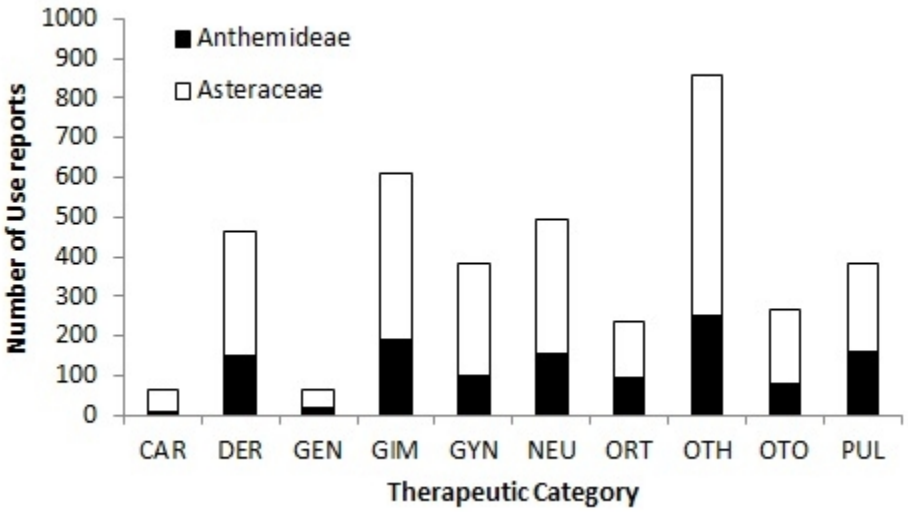


Figure 3 - Number of medicinal use reports by therapeutic category among Anthemideae species (black bars) and all Asteraceae species (complete bars). The percentage of Asteraceae use reports attributed to Anthemideae species is indicated above each category. Ten medicinal therapeutic categories are listed as in Moerman (1991) and defined in Supplemental Data.

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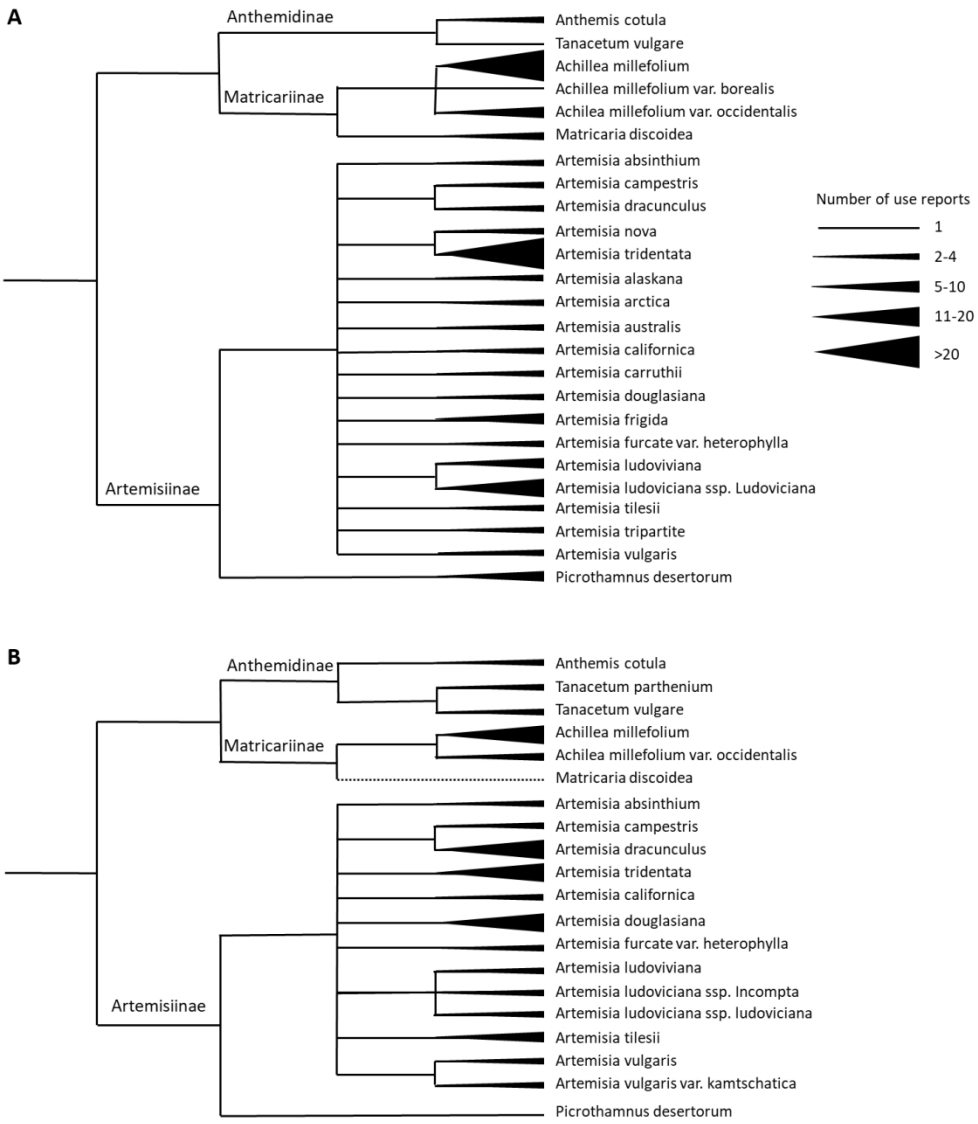


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