ETHNOPHARMACOLOGY OF THE ASTERACEAE FAMILY IN MEXICO
LA ETNOFARMACOLOGÍA DE LA FAMILIA ASTERACEAE EN MÉXICO

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Abstract
Background: In Mexico, the Asteraceae are part of traditional knowledge where its members have several uses, but they are particularly remarkable in traditional medicine and are used for different purposes.

Questions: What pharmacologically studies have been carried out with Asteraceae species used in Mexican traditional medicine? What pharmacological activities have been tested? What compounds are responsible for the tested activities?

Species studied: Asteraceae species used in Mexican traditional medicine pharmacologically tested.

Methods: A database including scientific studies on Asteraceae species which studies on pharmacological activity or phytochemical characterization was compiled and analyzed.

Results: From 249 reviewed studies only 202 fulfilled the criteria for our analysis. A total of 101 species distributed in 65 genera and 16 tribes were registered. The tribes Heliantheae and Senecioneae were the most studied. Ageratina pichinchensis, Artemisia ludoviciana, Heliopsis longipes, and Heterotheca inuloides were the most studied species. In Mexico, the Asteraceae family is mainly used in the treatment of diseases or symptoms related to the digestive and respiratory systems. In 48 % of the studies some biocidal activity was evaluated but only 21.8 % included phytochemical characterizations.

Conclusions: The antimicrobial activity and phytochemical characterizations are the main kind of ethnopharmacological studies for Asteraceae in Mexico. Most of the compounds responsible for the activities have not been identified yet. The uses of Asteraceae in Mexico are similar to other countries emphasizing its cultural importance in the world. Mexican Asteraceae should be prioritized in conservation and bioscreening schemes.

Key words: Compositae, ethnobotany, herbal medicine, natural compounds, traditional knowledge.

Resumen
Antecedentes: En México la familia Asteraceae es parte del conocimiento tradicional, sus miembros tienen varios usos, especialmente en la medicina tradicional con diferentes propósitos.

Preguntas: ¿Qué estudios farmacológicos se han realizado con especies de Asteraceae usadas en la medicina tradicional mexicana? ¿Cuáles son las actividades farmacológicas comprobadas? ¿Cuáles son los compuestos responsables de las actividades comprobadas?

Especies en estudio: Especies de Asteraceae usadas en la medicina tradicional mexicana probadas farmacológicamente.

Métodos: Se construyó y analizó una base de datos con estudios de asteráceas en los que se realizaron caracterizaciones fitoquímicas o estudiaron actividades farmacológicas.

Resultados: De 249 estudios revisados solo 202 cumplieron los criterios de inclusión del análisis. Se registraron 101 especies distribuidas en 65 géneros y 16 tribus. Heliantheae y Senecioneae fueron las tribus más estudiadas. Ageratina pichinchensis, Artemisia ludoviciana, Heliopsis longipes y Heterotheca inuloides fueron las especies más estudiadas. En México, la familia Asteraceae se utiliza principalmente en el tratamiento de enfermedades o síntomas relacionados con los sistemas digestivo y respiratorio. El 48 % de los estudios evaluó alguna actividad biocida y el 21.8 % incluyen caracterizaciones fitoquímicas.

Conclusiones: La actividad antimicrobiana y caracterizaciones fitoquímicas son los principales estudios realizados con asteráceas mexicanas. La mayoría de los compuestos responsables de las actividades farmacológicas evaluadas aún no han sido identificados. Los usos de Asteraceae en México son similares a los de otros países, lo que resalta su importancia cultural en el mundo. Las Asteraceae mexicanas deben ser priorizadas en planes de conservación y en estudios de bioprospección.

Palabras clave: Compositae, compuestos naturales, conocimiento tradicional, etnobotánica, herbolaria.
Ethnopharmacology of Asteraceae in Mexico

Historically, the plant kingdom has been the best source of remedies for a variety of diseases and pain. Plants are primary therapeutic agents used for treating illness, an integral element of health care systems, and the best testimony of cultural importance (Mata et al. 2019). In many cultures, plants are elemental for ancient traditional medicine systems and continue enriching our modern knowledge of herbal medicine. Therefore, medicinal plants have a fundamental role in the maintenance of global human health (Egamberdieva & Teixeira da Silva 2015). Traditional medicine is part of the evolutionary process where humans and plants interact; communities and individuals continue to discover practices and transforming techniques. Many modern drugs have origin in ethnopharmacology and traditional medicine (Helmsädter & Stagier 2014). Pharmacetical and scientific communities have paid particular attention to medicinal plants; numerous studies have validated the traditional use of plants and characterized phytochemically large species (Salazar-Aranda et al. 2013, Buenz et al. 2018).

The Mexican diversity of vascular plants has been estimated at 23,314 species (Villaseñor 2018), and more than 50 % are endemic to the country. More than 3,000 are used as medicinal plants but only a small proportion (1-2 %) has been studied (Villaseñor 1993, Espeso-Serna et al. 2004, Salazar-Aranda et al. 2013). Many members of Asteraceae are part of the traditional knowledge of our country where they are used as food, live fences, construction materials, and source of oils, insecticides, and garden ornamentals; however, they are specially used in traditional medicine (Heinrich et al. 1998, Leonti et al. 2003, Canales et al. 2005, Paredes-Flores et al. 2007, Estrada-Castillón et al. 2012, Gómez 2012, Ávila-Uribe et al. 2016, Casas et al. 2016, Vibrans 2016, Lara Reimers et al. 2019).

The Asteraceae or Compositae is one of the largest and most diverse families, comprising 10 % of all flowering plant species, rivaled only by Orchidaceae and Fabaceae (Mandel et al. 2019). It includes between 950 and 1,450 genera, with an estimated 25,000 to 35,000 species in the world and is the richest family of Mexican flora in genera and species (Villaseñor 2016, Mandel et al. 2019). Mexico is considered a center of diversification of this family with 417 genera and 3,113 species and it is the richest country for the family in Neotropics (Villaseñor 2018). Its wide distribution, from sea level (dunes or coastal vegetation) to the mountains, is attributed to its excellent dispersal capacity, genetic plasticity, and the presence of a wide variety of secondary metabolites synthesized as a protection strategy against predators or competitors (Villaseñor 2018). The members of Asteraceae are identified by inflorescences arranged in a capitulum or head, surrounded by an involucre with involucral bracts or phyllaries. On the capitulum there are two kinds of flowers: the outermost or ray flowers and the central or disc flowers. All the flowers are gamopetalous and lack of calyx or modified in a variable and peculiar structure called pappus (Villaseñor 1993). Due to its diversity, the Asteraceae family is divided in 36-38 tribes (Funk et al. 2005). In Mexico, there are 24 tribes of native species and two (Arctotideae and Calenduleae) of introduced species (Villaseñor 2018).

The vast diversity in Asteraceae is reflected in the presence of different bioactive compounds important for the pharmaceutical industry too (Kostić et al. 2020). Members of Asteraceae are known by their pharmacological activities as antibacterial, anti-inflammatory, wound-healing, anti-hemorrhagic, antipyretic, hepatoprotective, anti-tussive, antitumor, antiparastic, and antispasmodic (Carvalho et al. 2018, Panda & Luyten 2018). Several species are used in Mexican traditional medicine since its antibacterial properties (Sharma et al. 2017) and they are mainly used in the treatment of gastrointestinal, respiratory, and dental infectious diseases (Heinrich et al. 1998, Murillo-Álvarez et al. 2001, Hernández et al. 2003, Leonti et al. 2003, Canales et al. 2005, Paredes-Flores et al. 2007, Alonso-Castro et al. 2011, Rosas-Piñón et al. 2012, Sharma et al. 2017, Lara Reimers et al. 2019). Some of the most popular medicinal plants used in México are estafiate (Artemisia ludoviciana), Mexican arnica (Heterotheca inuloides), zoapatle (Montanoa tomentosa), and cempazúchitl (Tagetes erecta).

More than 5,000 compounds have been identified in Asteraceae, generally associated with some pharmacological activity. The presence of sesquiterpene lactones (SQLs), diterpenes, triterpenes, inulin-type fructans, polycytylenes, pentacyclic triterpene alcohols, benzofurans, flavones, flavonoids, and unsaturated fatty acids are common compounds in Asteraceae (Heywood et al. 1977a, b, Calabria et al. 2009). The SQLs are the major chemical compounds in Asteraceae, with at least 3,000 known structures involved in the defense against herbivores and parasites The SQLs, acetylenic compounds, and inulin-type fructans are as characteristic of Asteraceae as their inflorescences (Heywood et al. 1977a, b, Heinrich et al. 1998).

Despite the discovery of several secondary metabolites in Asteraceae, they attracted disproportionately little attention in the context of ethnopharmacological research, resulting in few systematic explorations and few commer-
In this review we answer the following questions: What pharmacologically studies have been carried out with Asteraceae species used in Mexican traditional medicine? What pharmacological activities have been tested? What compounds are responsible for the tested activities? The goal of our research was to synthesize the knowledge of the ethnopharmacology of the Asteraceae in Mexico.

Materials and methods

We conducted systematic searches for scientific studies of the pharmacological activity, or the phytochemical characterization of Asteraceae used in Mexican traditional medicine. The information was collected from scientific databases including ScienceDirect, Springerlink, Scopus, PubMed, Redalyc, Scielo, EBSCO, ACS Publications, BioMed Central, and Wiley online library, for entries published from 1983 to 2020. The keywords for our searches included: Mexican Asteraceae, medicinal Asteraceae, asteráceas mexicanas, asteráceas medicinales, Mexican traditional medicine, Asteraceae, Compositae. We only include studies that provide information on the collection site, the part used, the species identified, and the herbarium specimen, as recommended by the Guidelines on Good Herbal Processing Practices for Herbal Medicines (WHO 2018).

Species were classified based on the tribe scheme for Mexican Asteraceae by Villaseñor (2018). The nomenclature was based on taxonomic studies for the family including Ortiz-Bermúdez et al. (1998), Cabrera (2001), Funk et al. (2009), Estrada-Castillón & Villarreal-Quintanilla (2010), Schilling & Panero, 2011, Villaseñor & Ortiz (2012), García-Sánchez et al. 2014, Redonda-Martín (2017), Redonda-Martín (2020), and Villarreal-Quintanilla et al. (2020). To identify the native species to Mexico, the studies of Sosa & De-Nova (2012) and Villaseñor (2016) were consulted. The information was arranged alphabetically by tribe, genus, species, traditional uses, and pharmacological/phytochemical studies.

Results

A total of 249 studies where pharmacological activities and/or phytochemical characterizations were assessed for Asteraceae were found. The analysis of the information was carried out with 202 studies that fulfilled the recommendations of the Guidelines on Good Herbal Processing Practices for Herbal Medicines (Appendix 1). Forty-seven studies were not included since they were conducted with parts of plants (leaves, roots, etc.) or plant material purchased or acquired from laboratories, markets, supermarkets or they did not provide information about herbarium specimen.

A total of 101 species with ethnopharmacological and/or phytochemical studies from 16 tribes and 65 genera were recorded. Heliantheae has been the most studied tribe with 30 species and 19 genera, followed by Senecioneae with 17 species and seven genera (Appendix 1). The remaining tribes registered less than 10 species. The states

Figure 1. Number of collections by state of Mexican Asteraceae with ethnopharmacological studies.
where the specimens were collected are Morelos (23), Estado de Mexico (20), Puebla (11), Mexico City (10), San Luis Potosi (10), Nuevo Leon (10), and Veracruz (10). Yucatan and Jalisco are less explored by one mention each one (Figure 1).

The traditional uses referred in the reviewed studies are mainly on diseases or symptoms related to the digestive system (20.73 %), followed by treatment of different types of pain (15 %), and for the treatment of diseases associated to the respiratory system (10.2 %). Other uses were anti-inflammatory (7.6 %), and skin infections (7.3 %) (Table 1, Appendix 1). From the 202 reviewed studies, 62 (30.7 %) analyzed antibacterial activity and 44 (21.8 %) were phytochemical characterizations. Other assessed activities were cytotoxicity (12.4 %) and anti-inflammatory (7 %). Some activities, such as healing, diuretic, antimalarial, aphrodisiac, immunostimulant, among others, were evaluated only once. From 101 species, 21 were evaluated for their antibacterial activity, 13 were only characterized phytochemically, and five to assess their analgesic activity. Thirty-nine were studied only once. The most studied species have been Heliopsis longipes (18 studies, Figure 2C), Ageratina pichinchensis (16, Figure 2A), Artemisia ludoviciana (13, Figure 2B), and Heterotheca inuloides (10, Figure 2D). These species were mentioned in the 28.1 % of the reviewed studies. According to their distribution, 54 species are native to Mexico, 41 are endemic, and five are introduced. The Heliantheae presented the highest proportion of native (13) and endemic (17) species, followed by Senecioneae with five native and 12 endemics ( Appendix 1).

**Discussion**

Traditional knowledge is the best evidence of the efficacy of medicinal plants in treating diseases, their symptoms, and other ailments (Firenzuoli & Gori 2007, Helmstädtner & Staiger 2014). Ethnobotany and traditional knowledge

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**Table 1. Traditional uses and ethnopharmacological studies of Asteraceae in Mexico**

<table>
<thead>
<tr>
<th>Traditional use (illness/affection/symptom)</th>
<th>Mentions in the reviewed studies % (*)</th>
<th>Activity evaluated</th>
<th>Studies performed % (*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders/diseases: diarrhea, stomachache, dysentery, gastritis, indigestion, vomit, dyspepsia, deworming, lack of appetite, tapeworm, purge</td>
<td>20.73 (57)*</td>
<td>Antibacterial</td>
<td>30.7 (62)*</td>
</tr>
<tr>
<td>Aches, pain, analgesic, toothache, lumbago, migraine</td>
<td>15 (41)*</td>
<td>Phytochemical characterization</td>
<td>21.8 (44)*</td>
</tr>
<tr>
<td>Respiratory infections: cough, bronchitis, expectorant, flu, tuberculosis, cold, asthma</td>
<td>10.2 (28)*</td>
<td>Cytotoxicity</td>
<td>12.4 (25)*</td>
</tr>
<tr>
<td>Anti-inflammatory, neuritis, bruises</td>
<td>7.6 (21)*</td>
<td>Antifungal</td>
<td>8.0 (16)*</td>
</tr>
<tr>
<td>Skin infections: welts herpes, sores, scabies, skin wounds, baby rash, dermatophytosis, astringent</td>
<td>7.3 (20)*</td>
<td>Anti-inflammatory</td>
<td>7.0 (14)*</td>
</tr>
<tr>
<td>Fever</td>
<td>5.1 (14)*</td>
<td>Antiprotozoal</td>
<td>4.95 (10)</td>
</tr>
<tr>
<td>Colic, spasmyotic</td>
<td>4 (11)*</td>
<td>Spasmolytic</td>
<td>4.95 (10)*</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.6 (10)*</td>
<td>Antioxidant</td>
<td>4.46 (9)*</td>
</tr>
<tr>
<td>Anxiolytic</td>
<td>2.2 (6)*</td>
<td>Antimicrobial</td>
<td>3.96 (8)*</td>
</tr>
<tr>
<td>Labor</td>
<td>2.2 (6)*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Number of mentions in the reviewed studies.
about the preparation and administration of medicinal plants provide valuable information around active compounds. Several phytochemical compounds with biological activities were discovered from traditional knowledge and they have been a starting point for new therapeutics (Salazar-Aranda et al. 2013, Buenz et al. 2018). From the 122 plant-derived chemical products currently used in medicine, 80% are used congruently to their ethnomedical application (Saslis-Lagoudakis et al. 2011). These compounds have played a crucial role in treating and preventing human diseases. The artemisinin drug against parasitic diseases such as malaria was isolated from Artemisia annua used in traditional medicine for the treatment of respiratory diseases (Helmständter & Staiger 2014, Helmständter 2017). This is a prominent example of how the traditional knowledge regarding medicinal plants plays a key role in the identification of new bioactive agents or new drugs.

Ethnopharmacology of the Asteraceae in Mexico. Heliantheae, Senecioneae, Eupatorieae, and Astereae are the tribes with the highest number of genera and species in Mexico (Villaseñor 2018) and they are well represented in the reviewed ethnopharmacological and phytochemical studies. The species of Heliantheae and Senecioneae are the most evaluated and include most of the endemic studied species. On the other hand, from 26 tribes in México only 16 are represented in ethnopharmacological studies, possibly because some of them have a few species (e.g., Arctotideae, Chaenactideae, Gochnatieae, Liabeae, Onoserideae). But other tribes, such as Astereae and Eupatorieae are among the largest tribes in Asteraceae, with well-recognized species in Mexican traditional medicine. However, genera like Ageratina, Conyza, Erigeron, Eupatorium, Gymnosperma, Solidago, and Stevia, among others, are scarcely represented in ethnopharmacological studies.

From the best represented species in Mexican ethnopharmacological studies Ageratina pichinchensis (Figure 2A), named axihuítol or manrrubio, is a plant widely used in Mexican traditional medicine, whose pharmacological activities have been confirmed in preclinical and clinical studies (Aguilar-Guadarrama et al. 2009, Sánchez-Mendoza et al. 2013, Romero-Cerecero et al. 2017). This species is used in the treatment of diseases caused by or related to fungal and skin infections, wounds, and to treat pain and gastric ulcers (Aguilar-Guadarrama et al. 2009, Sánchez-Mendoza et al. 2013, Romero-Cerecero et al. 2017). Additionally, A. pichinchensis has wound healing, antiulcer, gastroprotective, antinociceptive, and anti-inflammatory effects (Sánchez-Mendoza et al. 2010, Romero-Cerecero et al. 2012a, Romero-Cerecero et al. 2013, Sánchez-Mendoza et al. 2013). Pharmacological evaluations showed that its extracts exhibit antifungal activity against Trichophyton mentagrophytes, T. rubrum, and Candida albicans (Ríos et al. 2003), and have shown therapeutic and mycological effectiveness in patients with vulvovaginal candidiasis (Romero-Cerecero et al. 2017). The antimicrobial activity of encecalin, taraxerol, β-sitosterol, and stigmasterol isolated from this species has been demonstrated (Aguilar-Guadarrama et al. 2009). The antinociceptive activity and gastroprotective effect of A. pichinchensis are related to the presence of 3,5-diprenyl-4-hydroxyacetophenone (HYDP) isolated from its leaves (Sánchez-Mendoza et al. 2013). Studies showed that 7-O-(β-D-glucopyranosyl)-galactin is the compound associated with the effects of A. pichinchensis in cell proliferation and healing activity in skin lesions in an animal model of diabetes (Romero-Cerecero et al. 2013, Romero-Cerecero 2014). The healing properties of A. pichinchensis have been assessed in human clinical trials. It has demonstrated effectiveness in the treatment of chronic venous leg ulcers (Romero-Cerecero et al. 2012a), and diabetic foot ulcers (Romero-Cerecero et al. 2015b).

Artemisia ludoviciana (Figure 2B) has been used in Mexican traditional medicine since pre-Hispanic times. It is commonly named estafiate, ajenjo del país, azumate, or iztauhatl (Calzada et al. 2007, Estrada-Soto et al. 2012, Anaya-Eugenio et al. 2016). This species is widely used to treat gastrointestinal disorders as parasites, indigestion, diarrhea, and dysentery. Also, it is used in the treatment of colic, bronchitis, dandruff, inflammation, diabetes, antimarial, and analgesic (Calzada et al. 2007, Estrada-Soto et al. 2012, Anaya-Eugenio et al. 2016). Studies in animal models have described antidiarrheal and antispasmodic activities of the essential oil obtained from aerial parts from A. ludoviciana (Said Fernández et al. 2005, Calzada et al. 2010, Estrada-Soto et al. 2012). Leaf extracts from this plant have antimicrobial activity against microorganisms responsible for gastrointestinal diseases such as Entamoeba histolytica, Escherichia coli, Giardia lamblia, Vibrio cholerae, and other responsible for infectious diseases as Candida albicans, Pseudomonas aeruginosa, and Staphylococcus aureus (Navarro et al. 1996, Said Fernández et al. 2005, Damián-Badillo et al. 2008). Most relevant is the activity of A. ludoviciana against Helicobacter pylori, the major etiological agent of chronic gastritis and peptic ulcer disease linked to gastric carcinoma (Castillo-Juárez et al. 2009). It has been documented its anti-Mycob-
bacterium tuberculosis activity (Jiménez-Arellanes et al. 2003). However, the compounds responsible for the mentioned antimicrobial activities have not elucidated yet. Additionally, Anaya-Eugenio et al. (2014) demonstrated the hypoglycemic and antihyperglycemic effects of arglanin and salvinine isolated from A. ludoviciana in mice, which supports its effectiveness in the treatment of diabetes in folk medicine.

Heliopsis longipes (Figure 2C), named chilcuague, chilcuán, pelitre, raíz de oro, and pyrethrum; it is endemic to the Sierra Gorda and Sierra de Álvaro in the limits of the states of Guanajuato, San Luis Potosí, and Querétaro (Cilia-López et al. 2008). This species is employed to calm toothaches, muscle aches, arthritis, rheumatism, as anti-inflammatory, in the treatment of oral herpes, oral infections, deworming, diarrhea, and muscle soreness (Cilia-López et al. 2008). It has antibacterial activity against Escherichia coli, as well as antifungal and anti-aflatoxigenic activity (Molina-Torres et al. 1999, Buitimea-Cantúa et al. 2020). The anti-inflammatory, antinociceptive, and anti-arthritis activities of H. longipes have been demonstrated in animal models (Acosta-Madrid et al. 2009, Hernández et al. 2009).

Figure 2. Most studied Asteraceae in the Mexican ethnopharmacology. A) Ageratina pichinchensis (Eupatorieae), B) Artemisia ludoviciana (Anthemideae), C) Heliopsis longipes (Heliantheae), D) Heterotheca inuloides (Astereae). Images from Enciclovida. Credits: A) Neptali Ramírez Marcial, C) Arturo de Nova, D) Bodo Nuñez Oberg.
2009, Cariño-Cortés et al. 2010, Cilia-López et al. 2010, Arriaga-Alba et al. 2013, Escobedo-Martínez et al. 2017, de la Rosa-Lugo et al. 2017). It has been demonstrated that its anti-inflammatory and anti-arthritic activities are higher than the reference drug phenylbutazone. Moreover, its extracts prevent the occurrence of secondary lesions, this makes it a better alternative for this type of chronic condition (Escobedo-Martínez et al. 2017). These biological activities are attributed to affinin, the main bioactive compound present in the roots of *H. longipes* (Molina-Torres et al. 1999). Ríos et al. (2007) established that the GABAergic system is involved in the analgesic response of affinin in *H. longipes* and de la Rosa-Lugo et al. (2017) indicate that it can be used for the treatment of orofacial pain. Affinin also induces the vasodilation showing its therapeutic potential in the treatment of cardiovascular diseases (Castro-Ruiz et al. 2017). In addition, the antimutagenic activity of affinin has been demonstrated (Cariño-Cortés et al. 2010, Arriaga-Alba et al. 2013).

*Heterotheca inuloides* (Figure 2D) is one of the most used plants in Mexican traditional medicine with a high market demand. It is commonly named Mexican arnica,

**Figure 3.** Some important Asteraceae to the ethnopharmacology in Mexico. A) *Chrysactinia mexicana* (Tageteeae), B) *Hofmeisteria schaffneri* (Eupatorieae), C) *Iosthephane heterophylla* (Heliantheae), D) *Parthenium hysterophorus* (Heliantheae). Images from Enciclovida. Credits: A) Arturo Cruz, B) Ignacio Vargas, C) Guillermo Ibarra, D) Aaron Balam.
acahual, cuauteteco, and xochiuepal (Rodríguez-Chávez et al. 2017). This species is widely used for the treatment of inflammatory conditions, skin wounds, fever, contusions, bruises, biliary disorders, cough, respiratory problems, gastritis, hemorrhoids, rheumatism, toothache, and urinary tract inflammation (Gené et al. 1998, Delgado et al. 2001, Rodríguez-Chávez et al. 2017, Egas et al. 2018). It has antibacterial activity against Helicobacter pylori and Streptococcus mutans and its flowers are effective against Giardia intestinalis trophozoites (Rosas-Piñón et al. 2012, Rodríguez-Chávez et al. 2015c, Egas et al. 2018). Several studies have assessed the anti-inflammatory and antioxidative activities of H. inuloides in different pharmacological models (Gené et al. 1998, Delgado et al. 2001, Maldonado-López et al. 2008, Egas et al. 2015, Rodríguez-Chávez et al. 2015a). The anti-inflammatory activity of H. inuloides has been associated with the presence of quercetin and sesquiterpenes (Delgado et al. 2001, Maldonado-López et al. 2008). The hepatoprotective and chemopreventive activities of H. inuloides are associated with the antioxidant activity of quercetin, one of the main compounds of this plant (Coballase-Urrutia et al. 2011, Ruiz-Pérez et al. 2014). The cytoxic properties, chelating, and tyrosinase inhibitory activity of H. inuloides have been described (Rodríguez-Chávez et al. 2017). Infusions of this plant showed antioxidant activity in vitro (Coballase-Urrutia et al. 2010, Rodríguez-Chávez et al. 2015a, Rodríguez-Chávez et al. 2015c).

Traditional medicinal uses and the pharmacological activities of compounds. Many studies on Asteraceae around the world focused on chemical analysis, have nearly isolated 7,000 different compounds (Panda & Luyten 2018). Ethnopharmacological studies have been useful in the identification of phytochemical compounds since they involve the characterization and isolation of compounds with pharmacological activity. The Asteraceae family in Mexican traditional medicine is mainly used in the treatment of gastrointestinal and respiratory diseases due to its antimicrobial activity (Murillo-Alvarez et al. 2001, Canales et al. 2005, Calzada et al. 2009, Salazar-Aranda et al. 2011, Rosas-Piñón et al. 2012, Robles-Zepeda et al. 2013). The use of this family in Mexico for the treatment of diseases related to the digestive system is similar to other countries as Nepal, New Zealand, and South Africa, where several of its species are used to treat infectious diseases (Saslis-Lagoudakis et al. 2011). The frequent use of Asteraceae as antimicrobial resources in different cultures highlights the importance of the family in the entire world and reveal cultural and chemical patterns where common traditional uses are similar in plant groups to treat related conditions or diseases.

The presence of secondary metabolites in Asteraceae as polyacetylenes and flavonoids with antibacterial and bacteriostatic activities, confirm the traditional medicine use of the family in the treatment of infectious diseases (Heinrich et al. 1998, Calabria et al. 2009). In the reviewed studies, some compounds with antimicrobial activities have been identified, especially those against bacteria causing infectious diseases, such as diarrhea, pneumonia, and tuberculosis. Research related to new natural antibiotics has a crucial worldwide interest, due to bacterial resistance. Microorganisms responsible for worrying and often fatal infections such as Candida albicans, Escherichia coli, Mycobacterium tuberculosis, Staphylococcus aureus, Streptococcus pneumonia, and Trypanosoma spp. are a worldwide concern, highlighting the importance of antibiotics research to treat these diseases (OMS 2016). Natural products have been a source of bactericides in traditional medicine, and they have been served as potential therapeutics against pathogenic bacteria since the golden age of antibiotics in the mid-20th century (Rossiter et al. 2017). However, the exploration of natural products as a source for new antibiotics has been greatly reduced over the past 20 years (Silver 2015).

The main pharmacological activity in the reviewed studies is antimicrobial. The ent-trachyloban-19-oic acid, isolated from the roots of Iostephane heterophylla (Figure 3C), is a potent antibacterial agent in the treatment of oral pathogens as Streptococcus mutans (Hernández et al. 2012). Two SQLs identified in Ambrosia confertiflora, santamarine and reynosin have bactericidal activity against Mycobacterium tuberculosis (Coronado-Aceves et al. 2016). Thymol esters of different short-chain fatty acids are the active principles for antimicrobial activity of Hofmeisteria schaffneri (Figure 3B) against Bacillus subtilis, Candida albicans, and Staphylococcus aureus, three of the main microorganisms responsible for several infections (Pérez-Vásquez et al. 2011). Essential oil and 5-(3-buten-1-yny)-2’, 2’-bithiény of Chrysactinia mexicana (Figure 3A) have antibacterial activity against Streptococcus pneumoniae, one of the major agents of infectious diseases of the respiratory tract and resistant to penicillin (Guevara Campos et al. 2011). The enecacalin and demethylencecalin isolated from Helianthella quinquenervis exhibited antifungal activity against Trichophyton mentagrophytes responsible for various skin infections (Castañeda et al. 1996). Ambrosin and incomptine B, two

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SQLs, isolated from *Parthenium hysterophorus* (Figure 3D) and *Decachaeta incompta* possess high trypanocidal activity. Both compounds are more effective than the current trypanocidal drugs used clinically (Sepúlveda-Robles et al. 2019).

Other pharmacological activities evaluated in the reviewed studies were cytotoxicity, anti-inflammatory, analgesic, antioxidant, and spasmylytic (Table 1). The Hofmeisterin III and other thymyl derivatives are the main antinociceptive agents from Hofmeisteria schaffneri (Figure 3B) (Angeles-López et al. 2010). In Callea ternifolia used in the treatment of diabetes, the chromenes 1 and 2, caelins A, and C compounds were identified. These compounds reduced the postprandial hyperglycemia, one of the most common abnormalities in the early phase of type 2 diabetes (Escandón-Rivera et al. 2017). Vernonia liatroides endemic to Mexico and used in menstrual disorders and dysentery, have been identified the sesquiterpenes α-methylene γ-lacton, which has muscle relaxant activity in animal models (Campos et al. 2003). Two species have been tested against cancer cell lines, Gonzalezia decurrens, which has displayed cytotoxic activity against colon cancer in vitro (Marquina et al. 2001), and Smalanthus maculatus, from which ursolic acid was isolated and showed cytotoxic activity against cancer cell lines (Jacobo-Herrera et al. 2016).

Limitations of the reviewed studies. In the current review, 43% of the studies report pharmacological activities but the responsible compounds have not been identified, and some species were studied only once. For example, Artemisia ludoviciana is one of the most studied species and its potent antimicrobial activity has been assessed, but the responsible compounds have not been identified. In the other hand, 8% of the studies are phytochemical characterizations where the pharmacological activity of the compounds was not assessed.

The WHO (2018) recommends that ethnomedical studies of medicinal plants should be supported by information of herbarium specimen, used part of the plant, traditional preparation, among others. However, in our review, 47 studies do not include information on herbarium specimens and or traditional uses, so the identification of the studied species cannot be corroborated. Providing this information is crucial, especially since the ultimate goal of ethnomedical studies is to ensure the safe and correct use of herbal remedies (Davidson et al. 2013, Helmstädter & Staiger 2014, Helmstädter 2017).

There are other impediments to using ethnomedical in the drug discovery process that limit the growth of herbal medicine as an industry to perform bioprospecting, as the generational loss of traditional medicine knowledge, loss of biodiversity, over-exploitation, and a historic lack of a legal framework on the use of medicinal plants (Buenz et al. 2018, Mata et al. 2019). In addition, studies on medicinal plants should involve a sustainable approach based on traditional knowledge, regulation, and quality control as essential points the development of a rational use of traditional medicine and herbal remedies (Buenz et al. 2018, Mata et al. 2019).

Acknowledgments

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## Appendix 1. Ethnopharmacological studies for the Asteraceae family in Mexico from 1983 to 2020.

<table>
<thead>
<tr>
<th>Tribu</th>
<th>Species</th>
<th>Ethnomedicinal use</th>
<th>Tested activity/study</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANTHEMIDEAE</strong></td>
<td>Artemisia absinthium L. (INT)</td>
<td>Stomach-ache, labor, colic, bile, diarrhea</td>
<td>Antibacterial, antiprotozoal</td>
<td>Hernández et al. (2003), Canales et al. (2005), Calzada et al. (2007)</td>
</tr>
<tr>
<td></td>
<td>Tanacetum parthenium (L.) Sch. Bip. (INT)</td>
<td>Convulsions, susto (fear), migraine, epilepsy, sedative, migraine, headache, rheumatoid arthritis, stomachache, toothache, analgesic, anti-inflammatory, antispasmodic</td>
<td>Antibacterial, anxiolytic, antidepressant</td>
<td>Hernández et al. (2003), Cárdenas et al. (2017)</td>
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<tr>
<td><strong>ASTEREA</strong></td>
<td>Baccharis conferta Kunth (NAT)</td>
<td>Cold, vomit, sickness</td>
<td>Antibacterial, anti-helmintic</td>
<td>Rocha-Gracia et al. (2011), Cortes-Morales et al. (2019)</td>
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<td></td>
<td>(Baccharis salicina Torr. &amp; A.Gray)</td>
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<td>Tribu</td>
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<td>Ethnomedicinal use</td>
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<tr>
<td>CALENDULEAE</td>
<td>Calendula officinalis L.</td>
<td>Analgesic, antiseptic, wound healing</td>
<td>Antibacterial</td>
<td>Rosas-Piñón et al. (2010), Rosas-Piñón et al. (2012)</td>
</tr>
<tr>
<td>CARDUEAE</td>
<td>Centaurea melitensis L.</td>
<td>Liver damage</td>
<td>Antitumoral</td>
<td>Torres-González et al. (2011)</td>
</tr>
<tr>
<td></td>
<td>Cosmos pringlei B.L. Rob. &amp; Fernald (END)</td>
<td>Stomachaches, toothaches, headaches, dysentery, improving circulation</td>
<td>Phytochemical characterization</td>
<td>Mata et al. (2002)</td>
</tr>
<tr>
<td>Tribu</td>
<td>Species</td>
<td>Ethnomedicinal use</td>
<td>Tested activity/study</td>
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<td></td>
<td>Brickellia cavanillesii (Cass.) A. Gray (END)</td>
<td>Diabetes, stomachache, liver diseases, diarrhea, cardiovascular diseases, treatment of ulcers, dyspepsia, analgesic, tapeworm, indigestion, colic, hypertension, anxiety</td>
<td>Vasorelaxing, anxiolytic, hypoglycemic</td>
<td>Aguirre-Crespo et al. (2005), Escandón-Rivera et al. (2012), Ávila-Villarreal et al. (2016)</td>
</tr>
<tr>
<td></td>
<td>Brickellia veronicifolia (Kunth) A. Gray (NAT)</td>
<td>Diabetes, gastroenteritis, diarrhea, pain, stomachache, biliary colic, dyspepsia, arthritis, topic inflammations, infectious diseases, gastritis</td>
<td>Hypoglycemic, antibacterial, analgesic, phytochemical characterization, anti-mutagenic, toxicity, spasmytic, antioxidant</td>
<td>Pérez-Gutiérrez et al. (1998), Pérez et al. (2000), Hernández et al. (2003), Pérez et al. (2004), Rivero-Cruz et al. (2006), Calzada et al. (2007), Palacios-Espinosa et al. (2008)</td>
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<td></td>
<td>Decachaeta incompta DC (NAT)</td>
<td>Diarrhea, dysentery</td>
<td>Antibacterial, antiprotozoal, trypanocidal</td>
<td>Calzada et al. (2009), Bautista et al. (2012), Velázquez-Domínguez et al. (2013), Sepúlveda-Robles et al. (2019)</td>
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<td></td>
<td>Hofmeisteria schaffneri (A. Gray) R.M. King &amp; H. Rob (END)</td>
<td>Skin wounds, fevers, gastrointestinal ailments, stomach aches, dyspepsia, bleeding diarrhea, topic antiseptic agent</td>
<td>Toxicity, analgesic, antifungal, antimicrobial, phytochemical characterization, spasmytic</td>
<td>Pérez-Vásquez et al. (2005), Pérez-Vásquez et al. (2008), Angeles-López et al. (2010), Pérez-Vásquez et al. (2011), Pérez-Vásquez et al. (2017)</td>
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<tr>
<td></td>
<td>Piqueria trinervia Cav. (NAT)</td>
<td>Typhus, fever, malaria, tetanus, diarrhea, antipyretic, abdominal pain</td>
<td>Antifungal, antibacterial, antiprotozoal, molluscicidal</td>
<td>Cruz-Reyes et al. (1989), Saad et al. (2000), Ruiz de Esparza et al. (2007), Rufino-González et al. (2017)</td>
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<td>Stevia salicifolia Cav. (NAT)</td>
<td>Gastrointestinal disorders</td>
<td>Phytochemical characterization</td>
<td>Mata et al. (1992), Meléndez-Rodríguez et al. (2002)</td>
</tr>
<tr>
<td></td>
<td>Gamochaeta americana (Mill.) (NAT)</td>
<td>Cough, cold, bronchitis, angina ache</td>
<td>Antibacterial</td>
<td>Rojas et al. (2001)</td>
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<td>(Gnaphallium americanum)</td>
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<td>Gnaphalium purpureum L. (NAT)</td>
<td>Cough, cold, bronchitis, angina ache</td>
<td>Antibacterial, cytotoxicity</td>
<td>Murillo-Álvarez et al. (2001)</td>
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<td>(Gnaphalium purpureum (L.) Cabrera)</td>
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<td></td>
<td>Gnaphalium attenuatum (NAT)</td>
<td>Respiratory illnesses</td>
<td>Antibacterial</td>
<td>Enciso-Díaz et al. (2012)</td>
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<tr>
<td></td>
<td>(Pseudognaphalium attenuatum (DC.) Anderb.)</td>
<td>Stomach diseases, swellings, wounds, prostatism, lumbago, neuritis, angina ache, blood pressure, diuretic, antipyretic, malarial</td>
<td>Spasmytic</td>
<td>Campos-Bedolla et al. (2005)</td>
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<td>Pseudognaphalium conoideum (Kunth) Anderb. (END)</td>
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<td>(Gnaphalium conoideum)</td>
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<tr>
<td><strong>HELENIEAE</strong></td>
<td><em>Helenium mexicanum</em> Kunth (NAT)</td>
<td>Antiseptic, acaricide, ster-</td>
<td>Antibacterial</td>
<td>Villagómez-Ibarra et al. (2001)</td>
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<td>mutative</td>
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<td><em>Ambrosia ambrosioides</em> (Cav.) W.W. Payne (NAT)</td>
<td>Wounds, sores, placental exp-</td>
<td>Antibacterial</td>
<td>Robles-Zepeda et al. (2013)</td>
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<td>ulsion, menstrual symptoms, hair diseases</td>
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<td><em>Ambrosia confertiflora</em> DC. (NAT)</td>
<td>Intestinal parasites, stomach-</td>
<td>Antibacterial, larvicial, cytotoxic</td>
<td>de la Torre Rodríguez et al. (2013), Robles-Zepeda et al. (2013), Coronado-Aceves et al. (2016)</td>
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<td>ache, fever, lack of appetite, menstrual symptoms</td>
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<td><em>Ambrosia psilostachya</em> DC. (NAT)</td>
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<td>Antibacterial, cytotoxicity</td>
<td>Murillo-Álvarez et al. (2001)</td>
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<td>*Dendroviguiera quinquera-</td>
<td></td>
<td>Cytotoxicity, antibacterial, phytochemical characterization</td>
<td>Villarreal et al. (1994)</td>
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<td>diata* (Cav.) E.E. Schill. &amp; Panero (END)</td>
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<td></td>
<td><em>Encelia laciniata</em> Vasey &amp; Rose (END)</td>
<td></td>
<td>Antibacterial, insecticide</td>
<td>Proksch et al. (1983)</td>
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<td>Encelia palmeri Vasey &amp; Rose (END)</td>
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<td>Antibacterial, insecticide</td>
<td>Proksch et al. (1983)</td>
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<td>Encelia ventorum Brandegee (END)</td>
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<td>Proksch et al. (1983)</td>
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<td>Flaveria trinervia (Spreng.) C. Mohr (NAT)</td>
<td>Diarrhea, dysentery</td>
<td>Antiprotozoal, antibacterial</td>
<td>Tapia-Pérez et al. (2003), Osuna et al. (2005)</td>
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<td>Flourensia cernua DC. (NAT)</td>
<td>Indigestion, expectorant, respiratory infections, tuberculosis</td>
<td>Antibacterial</td>
<td>Molina-Salinas et al. (2006), Molina-Salinas et al. (2011), Vásquez Rivera et al. (2014)</td>
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<tr>
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<td>Gonzalezia decurrens (A. Gray) E.E. Schill. &amp; Panero (END)</td>
<td>Infections, wounds, boils, and to alleviate gastric ulcers</td>
<td>Phytochemical characterization, cytotoxicity, insecticide</td>
<td>Marquina et al. (2001)</td>
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<td>(Viguiera decurrens A. Gray)</td>
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<td></td>
<td>Gonzalezia hypargyrea (Greenm.) E.E. Schill. &amp; Panero (END)</td>
<td>Gastrointestinal disorders</td>
<td>Cytotoxicity, anti-spasmodic, antibacterial, phytochemical characterization</td>
<td>Villarreal et al. (1994), Zamilpa et al. (2002)</td>
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<td>(Viguiera hypargyrea Greenm.)</td>
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<td></td>
<td>Helianthella quinquenervis (Hook.) A. Gray (NAT)</td>
<td>Deworming, gastrointestinal ailments, ulcers</td>
<td>Antibacterial, cytotoxicity, antifungal, antiprotozoal</td>
<td>Castañeda et al. (1996), Gutiérrez-Lugo et al. (1996), Calzada et al. (1998)</td>
</tr>
<tr>
<td></td>
<td>Iostephane heterophylla (Cav.) Hemsl. (END)</td>
<td>Arthritis, rheumatism, pain, diabetes, gastrointestinal ailments, dysentery, skin problems</td>
<td>Phytochemical characterization, antibacterial</td>
<td>Aguilar et al. (2001), Mata et al. (2001), Aguilar et al. (2007), Hernández et al. (2012), Ramirez et al. (2012), Rosas-Piñón et al. (2012)</td>
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<td>Montanoa grandiflora Alamán ex DC. (END)</td>
<td>Aphrodisiac, anxiolytic, labor</td>
<td>Anxiolytic, ejaculatory</td>
<td>Carro-Juárez et al. (2014), Rodríguez-Landa et al. (2014), Rodríguez-Landa et al. (2018)</td>
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### Ethnopharmacology of Asteraceae in Mexico

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<th>Species</th>
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<th>Tested activity/study</th>
<th>Studies</th>
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<tr>
<td><strong>INULEAE</strong></td>
<td><strong>Epaltes mexicana</strong> Less. (NAT)</td>
<td>Antibacterial</td>
<td>Phytochemical characterization, antibacterial</td>
<td>Kato et al. (1996)</td>
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<td><strong>NAASSAUVIEAE</strong></td>
<td><strong>Acourtia cordata</strong> (Cerv.) B. L. Turner (END)</td>
<td>Purge</td>
<td>Antibacterial</td>
<td>Rocha-Gracia et al. (2011)</td>
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<td><strong>(Perezia hebeclada</strong> (DC.) A. Gray)</td>
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<td><strong>Acourtia humboldtii</strong> (Less.) B.L. Turner (END)</td>
<td>Pain, rheumatism, renal, hepatic, gastrointestinal ailments, diabetes</td>
<td>Hypoglycemic</td>
<td>Martinez et al. (2017)</td>
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<p>| <strong>Chrysanthemum</strong>     | <strong>Montanoa tomentosa</strong> Cerv. (NAT)   | Aphrodisiac, anxiolytic, labor                                                     | Toxicity, aphrodisiac, anxiolytic, phytochemical characterization, ejaculatory       | Gallegos (1983), Southam et al. (1983), Carro-Juárez et al. (2004),  |
|                       | <strong>12Neurolaena oaxacana</strong> B.L. Turner (END) |                                                                                   |                                                                                        | Sollozo-Dupont (2015), Carro-Juárez et al. (2014), Estrada-Camarena et al. (2019), |
|                       | <strong>Parthenium hysterophorus</strong> L. (NAT) | Anti-inflammatory, insec-ticide, stomachache, fever, scabies, welts herpes        | Antibacterial, trypanocidal activity                                                  | Sánchez-Medina et al. (2001), Sepúlveda-Robles et al. (2019)          |
|                       | <strong>Parthenium tomentosum</strong> DC. (END)  | Gastrointestinal disorders                                                         | Spasmolitic                                                                           | Rojas et al. (1995)                                                   |
|                       | <strong>Perityle batopilensis</strong> A.M. Powell (END) |                                                                                   | Antibacterial, cytotoxicity                                                            | Gutiérrez-Lugo et al. (1996)                                          |
|                       | <strong>Tithonia diversifolia</strong> (Hems.l.) A. Gray (NAT) | Diabetes, skin infections                                                         | Anti-inflammatory, antibacterial, phytochemical characterization, hypoglycemic        | Bork et al. (1996), Villarreal-Ibarra et al. (2015)                    |
|                       | <strong>Verbesina abscondita</strong> Klatt (END)  | Respiratory illness                                                                | Antibacterial                                                                          | Rojas et al. (1991), Rojas et al. (1992)                               |
|                       | <strong>Viguiera dentata</strong> (Cav.) Spreng. (NAT) | Labor, baby rash, ant sting                                                        | Phytochemical characterization, antifungal, antimicrobial                             | Gao et al. (1985a), Peraza-Sánchez et al. (2005), Canales et al. (2008) |
|                       | <strong>Viguiera potosina</strong> S.F. Blake (END) |                                                                                   | Phytochemical characterization                                                         | Gao et al. (1985b)                                                    |
|                       | <strong>Xanthium strumarium</strong> L. (NAT)      |                                                                                   |                                                                                       |                                                                        |
|                       | <strong>Zonia grandiflora</strong> Nutt. (NAT)     | Anti-inflammatory                                                                  | Phytochemical characterization, analgesic                                             | Reves-Pérez et al. (2019)                                             |</p>
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<td><em>Psacalipopsis purpusii</em> (Greenm.) H. Rob. &amp; Brettell (END)</td>
<td>Anti-inflammatory</td>
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<td><em>Robinsonecio gerberifolius</em> (Sch. Bip.) T.M. Barkley &amp; J.P. Janovec (NAT)</td>
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<td><em>(Senecio angulifolius</em> DC., Senecio salignus DC.)</td>
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<td>Frei et al. (1998)</td>
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<td>(Dyssodia appendiculata Lag.)</td>
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<td>Dyssodia papposa (Vent.) Hitche (NAT)</td>
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<td>Gymnolaena oaxacana (Greenm.) Rydb (END)</td>
<td>Antimicrobial, cytotoxicity</td>
<td>Hernández et al. (2003)</td>
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<td>Pectis hankeana (DC.) Sch. Bip. (END)</td>
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<td>Porophyllum linaria (Cav.) DC (END)</td>
<td>Anti-inflammatory.</td>
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<td>Tagetes lucida Cav. (NAT)</td>
<td>Antimicrobial, antifungal, antidepressant, sedative, anxiolytic, analgesic, anti-inflammatory</td>
<td>Céspedes et al. (2006), Damian et al. (2008), Guadarrama Cruz et al. (2008), Guadarrama-Cruz et al. (2012), Rosas-Piñón et al. (2012), Bonilla-Jaime et al. (2015), Pérez-Ortega et al. (2016), González-Trijano et al. (2019), Monterrosas-Brison et al. (2019)</td>
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<td>Spasmyotic</td>
<td>Arroyo et al. (2004)</td>
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<td>Vernonia oaxacana Sch. Bip. ex Klatt (NAT)</td>
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<td>Rocha-Gracia et al. (2011)</td>
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<td>Vernonanthura patens (Kunth) H. Rob. (NAT)</td>
<td>Cytotoxicity, antitumoral</td>
<td>Avelino-Flores et al. (2019)</td>
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