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Review

Sanitary Registries and Popular Medicinal Plants Used in Medicines and Herbal Remedies in Mexico (2001–2020): A Review and Potential Perspectives

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Abstract: Mexico, a megadiverse country, hosts approximately 10–12% of the world's biodiversity and at least 21,989–23,424 vascular plants, 3350 of which are traditional medicinal flora. The Mexican Regulation categorizes herbal medicinal products into two groups: herbal medicines products and herbal remedies products. To date, there is no available information that describes and includes analyzed data about these two types of herbal medicinal products registered in Mexico. The purpose of the study was to analyze national sanitary registries of herbal products from 2001 to 2020 and identify native Mexican plants that are most used in herbal products. Further, the study aims to highlight the impact and relevance of this large number of medicinal plants, which represent a great source of information, genetic resources, bioactive compounds, and potential use in subsequent therapies based on scientific evidence. The future of medicines and herbal remedies is underestimated; thus, the significance of evaluating the great potential in studying plants for medicinal use must be taken into account.

Keywords: sanitary registries; popular medicinal plants; medicinal remedies; medicinal plants

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1. Introduction

Historically, herbal products were the first resource used by man for the improvement of his health. It is the knowledge of these products that perpetuated medicinal practices prevail today as well [1].

Mexico ranks fifth among megadiverse countries as it is home to nearly 23,424 vascular plants, which represent 5000 endemic plant species; of these, a total of 4500 medicinal plants have been estimated, while only 3000 are registered in the herbarium of the Mexican Institute of Social Security (IMSS). However, a pharmacological analysis of only 5% has been reported [2–5]. The country boasts a wide range of medicine made from plants that are representative of traditional Mexican herbal products [6,7]. There has been a steady rise in the use and commercialization of herbal products, demonstrative of the increase in world demand in this industry. Further, 90% of the population in Mexico has opted for these products at least once in their lives, as indicated by the Secretaría de Salud (SS) [1] and Comisión Federal para la Protección contra Riesgos Sanitarios (COFEPRIS) [8].

The World Health Organization (WHO) has mandated that its member countries, including Mexico, must certify the quality of the marketed plant species [9]. "WHO Strategy on traditional medicine 2002–2014" [10,11] describes the use, management, and

cultivation of medicinal plants, including issues related to the policy, safety, efficacy, quality, and rational use of natural resources used in traditional medicine [12]; the second update of this strategy is valid until 2023 [13].

The present review performed an analysis of sanitary registries in Mexico of herbal medicines and herbal remedies. Given the significant chemical biodiversity of Mexican plants and their medicinal value as natural products, we intend to influence the potential of the great chemical diversity of plants and herbal products in Mexico, presenting it as an underutilized resource by focusing on the large number of health registers in recent years, which have been increasing. The novelty is that the global analysis of sanitary registries in Mexico of herbal products offers valuable information about the diversity, uses, and formulations of these products. We made a reflection on relatively unexplored areas, such as genetic traits, agricultural properties, and medicinal quality.

2. Current Outlook Regarding the Use of Herbal Products in Mexico

In Mexico, approximately 50,000 shops were estimated to have sold herbal products and/or food supplements, with an economic spill annual of at least 2 million USD ($100,000 MXN) annually, as reported by the National Federation of the Industry of Herbalism and Alternative Medicine, Traditional and Naturist (FNIHMATN) [14]. However, the suggested amount is not inclusive of the total production chain; if it were, the figure would certainly increase by several zeros. This fact underlines the underrated importance of a branch of the health industry, as 8 out of 10 Mexicans use traditional medicine. Thus, for every 100 MXN spent for treatments with medicinal plants used by the population from 2008 to 2013, an average of $45.1 MXN could be calculated, as per the National Institute of Statistics and Geography (INEGI) [15].

The Mexican Regulation of Health Products categorizes herbal products into two groups: herbal medicines and herbal remedies. The former relates to medicines in general health that are made with plant material or its derivative and assume an aerial/underground part of a plant as its main ingredient, which may also make use of extracts, tinctures, juices, resins, fatty and essential oils, presented in pharmaceutical form, whose therapeutic efficacy and safety has been scientifically confirmed in the national or international literature (Ministry of Health, 2018, art. 224, Sect. B). The latter form of herbal medicinal products is defined in the Health Supplies Regulation (RIS) as the preparation of medicinal plants, or their parts (individual or combined) and their derivatives, presented in pharmaceutical form, which is known in traditional discourses of medicine to relieve some participating or isolated symptoms of the disease [16,17]. To date, there is no available information that describes and includes analyzed data about active principles and therapeutic indications of herbal remedies registered in Mexico.

3. Regulation of Herbal Products in Mexico

In 1997, the General Law of Health [18] in Mexico was reformed to include the concept of the "herbal product". However, the concept of herbal remedies specifically fails to appear in this law to date. According to the regulation of health products (RIS), the identity of the components and the scientific name of the plant(s) are necessary data required for the registration of an herbal remedy. In contrast, herbal medicine is required to present further information: pharmaceutical form, dose, route of administration, contraindications, adverse reactions, and pregnancy and pediatric use [17]. One analysis of the regulation for herbal products (medicine and remedies) in Mexico [16] outlines the fundamental difference between the two as the information that sustains efficacy and safety. Herbal medicine requires the presentation of this information when sanitary registration is requested; in contrast, herbal remedies only need to present safety information. The latter partially lacks efficacy issues, as has been demonstrated by traditional medicine.

In 2018, a guideline to evaluate new registries was generated by the Mexican government via the General Health Council of the Ministry of Health, which is responsible for coordinating the registering of these products using a mechanism that previously only

requested documentation and normative compliance to be presented [19]. This guideline established the criteria for assessment and opinion of past or new registries from herbal medicine using scientific evidence as support. After 2018, the evaluation included the intervention of a specific committee for herbal medicine and the presentation of clinical studies if necessary. The herbal medicine with a previously assigned active sanitary registry must update the documentation and clinical studies if applicable [9].

4. Sanitary Registries of Herbal Medicine and Herbal Remedies during 2001–2020 in Mexico

In the present review, we have analyzed the COFEPRIS database from the 2001–2020 period [8] of herbal medicine and herbal remedies with sanitary registries to investigate the basic aspects of their pharmacoepidemiology in Mexico. One of the primary results was the number of total registrations for herbal medicine and herbal remedies in the 20 years period, 241 and 129, respectively, with a mean of 12 and 6 registers per year, respectively. However, upon analyzing the number of sanitary registries, an ascending peak was observed during 2001 and 2005 in the number of registrations, which repeated in 2013 and 2018, with 73 registries in the case of herbal medicines and 71 registers for herbal remedies during 2012–2019. However, for herbal medicines in the period 2006–2012, the number of registrations was constant, up to five registries per year. In contrast, for herbal remedies during the period 2005–2011, an average of 2.5 registries per year was observed. It is interesting to note that there were no registrations in the herbal medicine section during 2017. Additionally, for herbal remedies, there were no registrations during 2002, 2004, and 2008. The year with the greatest number of herbal medicine and herbal remedies registrations was 2003 (n = 50, 21, respectively), while 2011 was the year with the lowest number of registries for herbal medicine (n = 1), with 2017 as an exception. These data are shown in Figure 1a, b. Throughout the analyzed period, a six-year phase from 2006 to 2012 was noted to characterize a considerable decrease in the number of herbal product registrations. This coincided with the period of government of the then-president, Vicente Fox Quesada, who, via Health Minister Julio Frenk Mora and Federal Commissioner of COFEPRIS, Ernesto Enriquez Rubio, started a "new comprehensive pharmaceutical policy" in 2015 [20]. With this new policy, the regulation ensured that "miracle products", which were drugs with misleading advertising and no scientific evidence, would not be sold in the country unless pharmaceutical laboratories presented scientific evidence that demonstrated that they proclaim or include active principles of the Herbal Mexican Pharmacopeia (FHEUM, for its acronym in Spanish). This situation may have triggered laboratories to considerably diminish their interest in channeling these types of products to the market. This may also have occurred as a result of COFEPRIS, due to lack of scientific evidence or non-compliance in tests, not approving the registration of diverse herbal products. Since 2012 and 2013, the registries continued growing with a notable decrease in 2017, coinciding with the publication of another regulatory document, an Official Mexican Standard (NOM, for its acronym in Spanish) concerning the "stability of active principles, drugs as well as herbal remedies" in 2016 [21].

4.1. Main Laboratories of Herbal Products

In the context of the registers obtained by each laboratory of herbal medicine after these 20 years, the laboratories with the largest number of registries are FITONAT (n = 26), BIOFARMA NATURAL (n = 16), and SALUD NATURAL M. (n = 16). The graph illustrates the top 10 laboratories (Figure 2a) in contrast with those that have a unique registry, such as INDEX OF MEXICO and SUANCA INDUSTRIES, among others. It may be worth noting that laboratories with the highest number of records of herbal medicine are of national origin, while there are also laboratories of foreign origin that work with branches of herbal medicine such as SCHWABE and WYETH, which have seven registries each, and ROCHE, NOVARTIS, and SCHERING PLOUGH, with two registers each. In the case of laboratories

with registries of herbal remedies, one laboratory was observed for each register in the 20-year period.

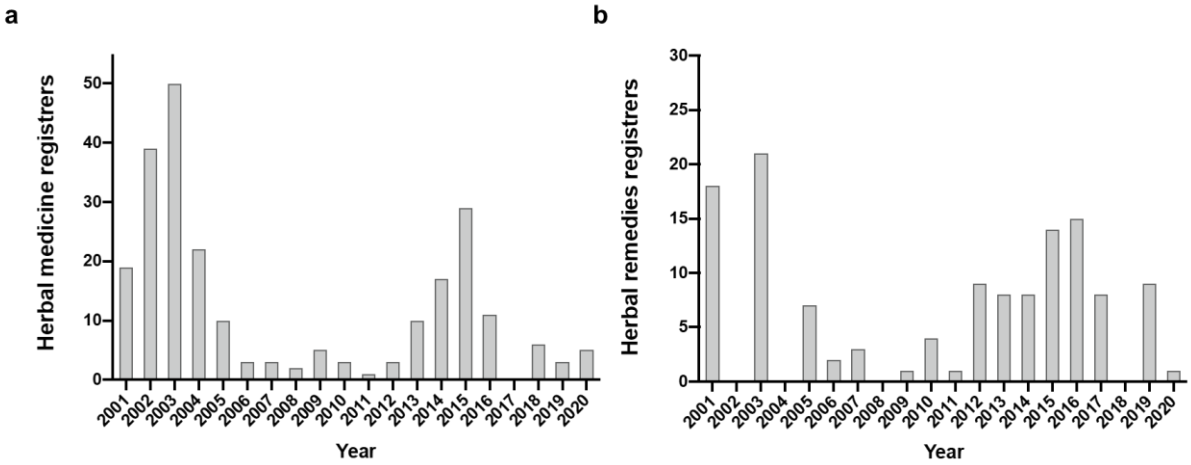

Figure 1. The number of (**a**) herbal medicine and (**b**) herbal remedies with sanitary registers in Mexico during 2001–2020. Data obtained from: COFEPRIS (Comisión Federal para la Prevención de Riesgos Sanitarios). 2022; Listados de Registros Sanitarios de Medicamentos. https://www.gob.mx/cofepris/documentos/registros-sanitarios-medicamentos (accessed on 12 August 2021).

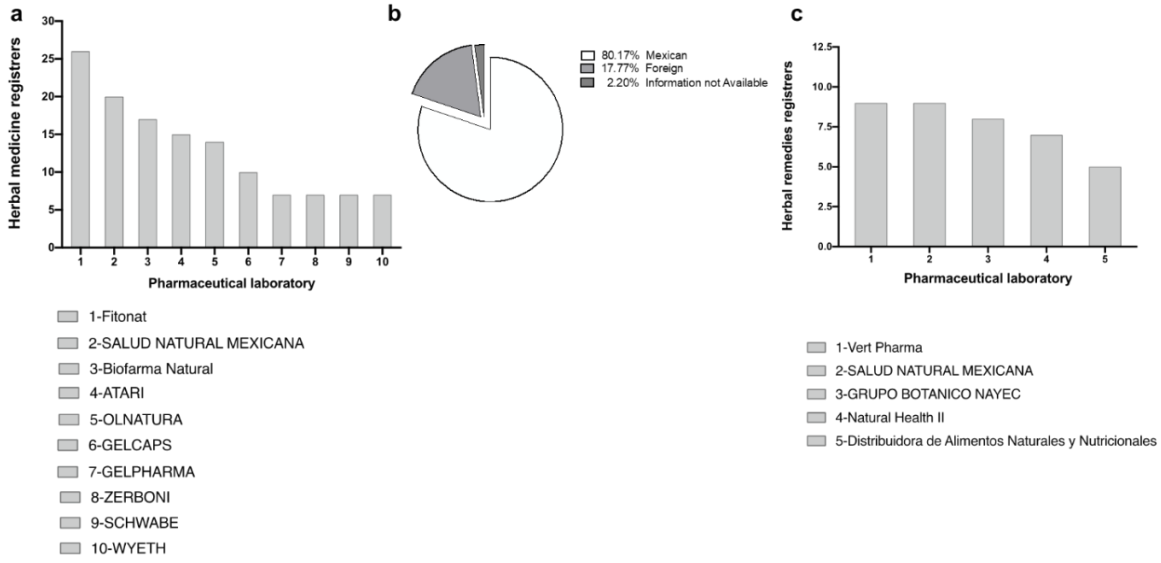

Figure 2. (**a**) The ten laboratories with the highest number of sanitary registries of herbal medicines in Mexico. (**b**) Origin of pharmaceutical laboratories with herbal remedies registers in Mexico. (**c**) The five laboratories with the highest number of sanitary registries of Herbal remedies in Mexico. The figures include all the registers in the period 2001–2020. Data obtained from: COFEPRIS (Comisión Federal para la Prevención de Riesgos Sanitarios). 2022; Listados de Registros Sanitarios de Medicamentos. https://www.gob.mx/cofepris/documentos/registros-sanitarios-medicamentos (accessed on 12 August 2021).

During these 20 years, 65 laboratories of herbal medicine ventured into the branch. It was found that most laboratories that produce this type of product are of national origin; out of 241 sanitary registries included in the analysis, 194 (80%) were submitted by Mexican laboratories, while the other 43 (17.8%) were submitted by foreign laboratories (Figure 2b). Through the years selected for analysis, the number of laboratories of national origin dominated the number of laboratories of foreign origin. In 2003, 45 registries were observed from national laboratories, while only five registries were noted from laboratories

of foreign origin. In 2016, only registries from laboratories of national origin were made. The 10 laboratories with the highest number of sanitary registrations, in addition to the percentage of Mexican and foreign laboratories, have been presented in Figure 2a,b.

In the evaluated period (2001–2020) for the herbal remedies of the 129 health registries, we identify a total of 65 laboratories, among which Vert Pharma (n = 9), SALUD NATURAL MEXICANA (n = 9), GRUPO BOTANICO NAYEC (n = 8), Natural Health II (n = 7), and Distribuidora de Alimentos Naturales y Nutricionales (n = 5) demonstrated the highest number of health registries; the top five are shown in Figure 2c. Laboratories with sanitary registries of herbal remedies were generally of Mexican nationality, a fact that is relevant during the comparison of information on registries for herbal medicines, wherein foreign laboratories may also be involved.

In the analysis, the origin of the pharmaceutical laboratories (national or foreign) was considered. As mentioned above, by 2018 in Mexico, 50,000 establishments were selling herbal products and/or food supplements, leading to a spill of at least 262 million USD. Undoubtedly, it is a market that is on the rise [22], supported by two important factors: the growing wave of the idea "the natural does not harm" and the multiple studies demonstrating the promising healing effects of these types of products [17–19]. As mentioned above, 80% of Mexicans have used traditional medicine at least once in their lives [23–25], which is a high percentage when compared with the USA (35%) [26] or Australia (63%) [27]. It is also intriguing to note that the origin of laboratories that decided to invest in herbal medicine, according to our study, were primarily national. Year after year, from 2001 to 2020, laboratories of Mexican origin far exceeded the acquisition of sanitary registers in comparison with foreign laboratories (79% vs. 19%). A reason for this may have been that national laboratories are more familiar with the market they deal with than others. In Mexico, the population relies on these herbal products for the recovery of an optimal state of health; however, in the Mexican market, it is assumed that a variety of miracle products still exist [8,23,28,29].

4.2. Pharmaceutical Forms of Herbal Products

Another aspect that was analyzed in the study is the pharmaceutical form used for each herbal medicine and herbal remedy. It was found that of the 241 registers, 96 (42.3%) promoted the use of capsules as a pharmaceutical form, followed by tablets (n = 41), suspensions (n = 22), powder (n = 17), and elixir (n = 9) for herbal medicine. Meanwhile, 123 registers were found for herbal remedies, 36 (29.3%) capsules, syrup (n = 20), solution (n = 17), and powder (n = 13). Of the pharmaceutical forms, the less used by the industry were liniments, patches, effervescent powders, ointments, chewable tablets, aerosols, and vials, as each of them had a single record. All the above-mentioned pharmaceutical forms can be seen in Figure 3a,b. Although our study confirms that a greater number of Mexican pharmaceutical laboratories have registries of herbal products in the last 20 years, most of the pharmaceutical forms are capsules, a fact that reveals limited pharmaceutical technology.

4.3. Therapeutic Indications for Herbal Products

The therapeutic indications that prompt the prescription of herbal products have been depicted in a bar graph, highlighting the five most frequent ones. The most frequent therapeutic indication for herbal medicine was found to be nutritional supplements with 57 registers, followed by digestive disorders (n = 42), anxiolytics (n = 29), vascular disorders (n = 29), and respiratory diseases (n = 25). In contrast, other therapies with only one register include antiseptic and weight control (Figure 4a). For the herbal remedies, the five most frequent therapeutic indications were respiratory diseases with 25 registers, anti-inflammatories (n = 20), anxiolytics (n = 16), information not available (n = 16), and digestive disorder (n = 14). Meanwhile, only one register was found for dermatological, antiseptic, analgesic, and eye care (Figure 4b).

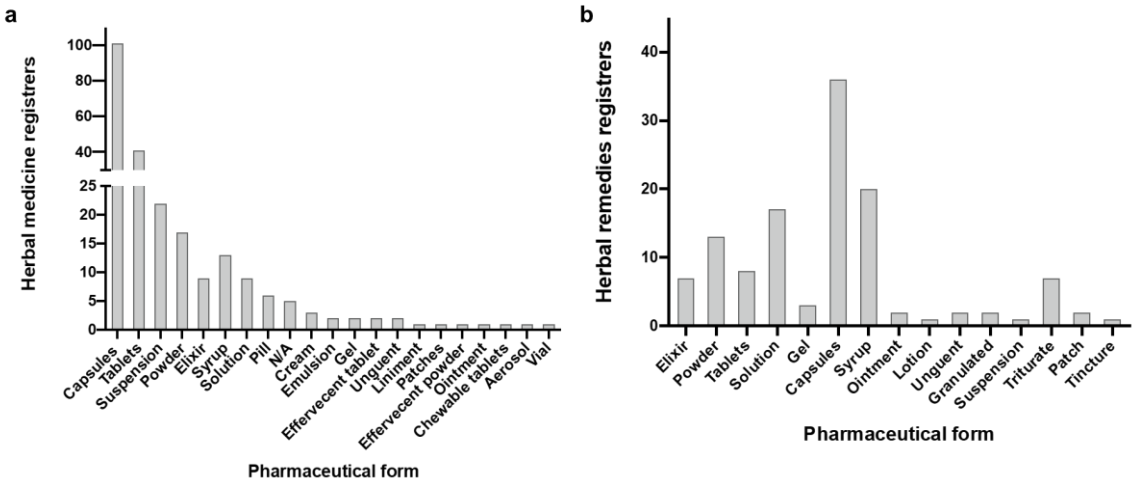

Figure 3. Pharmaceutical forms of (**a**) herbal medicines and (**b**) herbal remedies with sanitary registries in Mexico in the period 2001–2020. Data obtained from: COFEPRIS (Comisión Federal para la Prevención de Riesgos Sanitarios). 2022; Listados de Registros Sanitarios de Medicamentos. https://www.gob.mx/cofepris/documentos/registros-sanitarios-medicamentos (accessed on 12 August 2021).

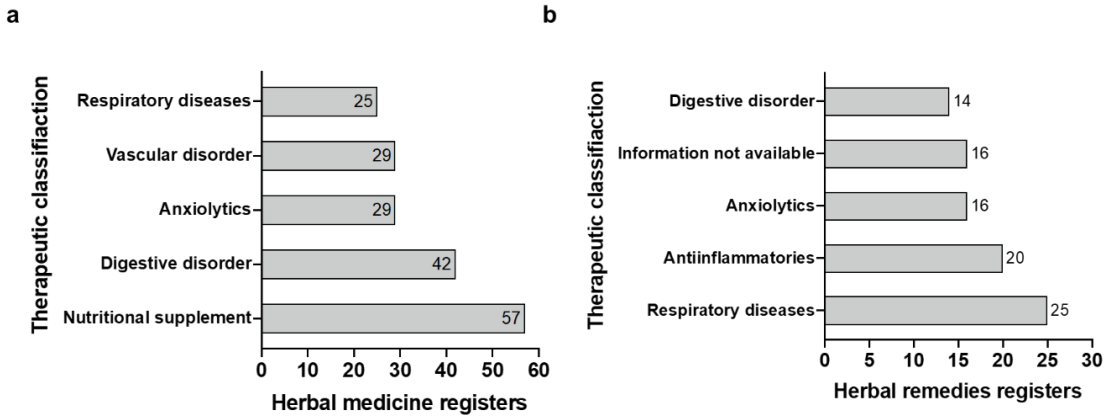

Figure 4. The five most frequent therapeutic indications of sanitary registries of (**a**) herbal medicine and (**b**) herbal remedies in Mexico during 2001–2020. Data obtained from: COFEPRIS (Comisión Federal para la Prevención de Riesgos Sanitarios). 2022; Listados de Registros Sanitarios de Medicamentos. https://www.gob.mx/cofepris/documentos/registros-sanitarios-medicamentos (accessed on 12 August 2021).

Although several medicinal plants have proven pharmacological properties, it is generally conceived, among regulatory agencies and within the scientific community, that herbal products are not "safe" or effective. This mistrust could be due to the "miracle products" offered by non-registered laboratories or misleading traditional healers. In our analysis, the most frequent therapeutic indication was nutritional supplement (23.6%) for herbal medicine and 19.3% for respiratory diseases in the case of herbal remedies. Despite the regulations on advertising for these types of products that generally prevent false marketing, the demand for consumption of weight loss products is high as members of the Mexican community popularly resort to this type of treatment to avoid alternatives such as diets and exercise [23,24]. In particular, the prevalence of self-medication for weight loss herbal products in Mexico has been reported as 42.9% [30].

Other frequent therapeutic indications in the present study were: digestive disorder, anxiolytics, vascular disorder, and anti-inflammatory, as opposed to the five most frequent morbidity causes in Mexico: acute respiratory infections, intestinal infections, urinary tract infections, digestive disorders, and gingivitis/periodontal disease [31]. A limited number

of these herbal products function against these common causes. However, since obesity and its complications are one of the principal causes of mortality, nutritional supplements focused on weight control match this disease from a certain point of view [31]. It is of great importance to identify the types of indications that are most encompassed by the pharmaceutical industries since they are proportional to the diseases or discomforts that primarily afflict the Mexican population or for those that most resort to the use of herbal products.

4.4. Popular Medicinal Plants Used for Herbal Products

Further, the most popular medicinal plant for herbal medicine showed that 59 registries (24.5%) reported the combination of different types of plants. In these products that report a combination, it is not specified which plants are used and if vitamins or other active components are added. On the other hand, the sole species that have the highest registration numbers of herbal medicine are *Ginkgo biloba* and *Panax ginseng* (n = 11 each), *Plantago psyllium* (n = 10), and *Hedera helix* (n = 9). In the Mexican and adjoining areas, the endemic plant with the greatest number of registers was *Serenoa repens,* which has six (2.5%) registries; however, there are only three herbal medicines that include a mixture of Mexican medicinal plants: *Persea gratissima*, *Sambucus* (registries did not include species of *Sambucus*, but it is assumed that Mexico has *Sambucus nigra* var. canadiensis, which is known as *Sambucus mexicana*), and *Phaseolus vulgaris*. In contrast, there are 41 (16.5%) registries of Asian plants, which are the most frequent origins of these medicinal plants.

In the case of herbal remedies, the five most used medicinal plants for the preparation of herbal remedies are: *Eucalyptus* (n = 14), *Agastache mexicana* (n = 9), followed by the mixture known as Bach Flowers (n = 8), *Gnaphalium oxyphyllum* (n = 7), and finally, *Amphipterygium adstringens* (n = 7). This is taken from a total of 100 medicinal plants reported in the 129 sanitary registries for the period 2001–2020.

Regarding the use of native medicinal plants in Mexico, a low percentage was found, suggesting that the majority of these products and the Mexican biodiversity are not being managed properly. This leads to a loss of opportunities to use the natural resources of the country in an adequate manner (Table 1).

Table 1. Medicinal plants with sanitary registries used in herbal medicines and herbal remedies.

Herbal Medicines	Origin	Sanitary Registries	(%) Sanitary Registries	Herbal Remedies (Continuation)	Origin	Sanitary Registries	(%) Sanitary Registries
Plants combined	N/A	59	24.5	*Heterotheca inuloides*	Asia and Europe	4	3.13
Ginkgo biloba	Asia	11	4.6	*Smilax cordifolia*	Mexico and South America	2	1.56
Panax ginseng	Asia	11	4.6	*Rosmarinus oxyacantha*	Europe	1	0.78
Silybum marianum	Africa	9	3.7	*Uncaria tomentosa*	South America	1	0.78
Plantago psyllium	Europe	10	4.1	*Mentha piperita*	Asia	2	1.56
Echinacea	North America	6	2.5	*Tila platyphyllos*	Europe	1	0.78
Serenoa repens	North America	6	2.5	*Crataegus*	Asia and Europe	2	1.56
Soybean (*Glycine max*)	Asia	6	2.5	*Olea europea*	Asia and Europe	1	0.78
Valeriana officinalis	Europe	6	2.5	*Tila mexicana*	Mexico	1	0.78
Hedera helix	Europe	9	3.7	*Casimiroa edulis*	Central and South America	1	0.78

Table 1. *Cont.*

Herbal Medicines	Origin	Sanitary Registries	(%) Sanitary Registries	Herbal Remedies (Continuation)	Origin	Sanitary Registries	(%) Sanitary Registries
Hypericum perforatum	Europe	5	2.1	*Tecoma stans*	Mexico	3	2.34
Plant + Vitamins	N/A	5	2.1	*Turnera diffusa*	Mexico and Central America	4	3.13
Aesculus	Europe	4	1.7	*Medicago sativa*	Asia	1	0.78
Cassia angustifolia	Africa	4	1.7	*Cassia senna*	Africa	2	1.56
Garcinia cambogia	Asia	4	1.7	*Peumus boldus*	South America	1	0.78
Matricaria chamomilla	Europe	4	1.7	*Matricaria recutita*	Asia and Europe	1	0.78
Cimicifuga racemosa	North America	3	1.2	*Salvia officinalis*	Asia	1	0.78
Passiflora incarnata	United States	3	1.2	*Jacobinia spicigera*	Mexico and South America	1	0.78
Rhodiola rosea	Europe	3	1.2	*Haematoxylun brasiletto*	South America	2	1.56
Vitis vinifera	Europe	3	1.2	*Aloe sp*	Africa	1	0.78
Activated carbon	N/A	2	0.8	*Eucalyptus*	Australian and Tasmanian	14	10.94
Amorphophallus konjak	Asia	2	0.8	*Ipomea purga*	Mexico	1	0.78
Coffea canephora	Africa	2	0.8	*Artemisa mexicana*	Mexico and North America	1	0.78
Cordia verbenacea	South America	2	0.8	*Cooperia*	South America	1	0.78
Cynara scolimus	Europe	2	0.8	*Uncaria tomentosa*	South America	1	0.78
Melissa officinalis	Europe	2	0.8	Flores de Bach	Asia and Europe	8	6.25
Pelargonium sidoides	Africa	2	0.8	*Alnus japonica*	Asia	1	0.78
Plantago ovata	Asia	2	0.8	*Phytolaca*	America and Asia	1	0.78
Vaccinium	Europe	2	0.8	*Cymbopogon nardus*	Asia	1	0.78
Arctium	Europe	1	0.4	*Panax ginseng*	China	2	1.56
Astragalus membranaceus	Asia	1	0.4	*Trichosanthis*	China	1	0.78
Camelia sinensis	Asia	1	0.4	*Agave centaury*	America	2	1.56
Camellia	Asia	1	0.4	*Populus tremula*	Africa, Asia and Europe	1	0.78
Cassia senna	Africa	1	0.4	*Larix decidua*	Asia and Europe	1	0.78
Centella asiática	Asia	1	0.4	*Carpinus betulus*	Asia and Europe	1	0.78
Cynara	Europe	1	0.4	*Olea europea*	Asia and Europe	1	0.78
Eleuteroccoccus perforatum	Asia	1	0.4	*Sinapis arvensis*	Europe	1	0.78
Eucalyptus globulus	Australia	1	0.4	*Gentiana amarella*	Asia, Europe, America	1	0.78

Table 1. *Cont.*

Herbal Medicines	Origin	Sanitary Registries	(%) Sanitary Registries	Herbal Remedies (Continuation)	Origin	Sanitary Registries	(%) Sanitary Registries
Fucus	Europe	1	0.4	*Zinnia elegans*	Mexico	1	0.78
Glycyrrhiza glabra	Africa	1	0.4	*Andrographis paniculata*	Asia	1	0.78
Grindelia robusta	United States	1	0.4	*Astragalus membranaceus*	Asia	1	0.78
Harpagophytum	Africa	1	0.4	*Capsicum annum*	Mexico, Central and South America	2	1.56
Humulus lupulus	Europe	1	0.4	*Malva parviflora*	Europe	2	1.56
Juniperus	North America	1	0.4	*Guazina ulmifolia*	Mexico and South America	1	0.78
Lavandula angustifolia	Europe	1	0.4	*Cimicifuga racemosa*	North America	1	0.78
Lepidium latifolium	Europe	1	0.4	*Cinnamomum*	Asia	1	0.78
Lytrum	N/A	1	0.4	*Gnaphalium oxyphyllum*	Asia and Europe	7	5.47
Marsdenia condurango	South America	1	0.4	*Crescentia alata*	Mexico	1	0.78
Olea europea	Europe	1	0.4	*Sambucus mexicana*	Mexico	1	0.78
Paullinia cupana	South America	1	0.4	*Lycopersicum esculentum*	Asia and Europe	1	0.78
Persea gratissima	Mexico	1	0.4	*Citrus*	Asia	6	4.69
Petasites hybridus	Europe	1	0.4	*Matricaria recutita*	Asia and Europe	1	0.78
Peumus boldus	South America	1	0.4	*Hedera helix*	Africa, Asia and Europe	1	0.78
Phaseolus vulgaris	Mexico	1	0.4	*Bougainvillea glabra*	Brasil	5	3.91
Phyllium plantago	Europe	1	0.4	*Gnaphalium sp*	America	1	0.78
Piper methysticum	Oceanía	1	0.4	*Pinus sp*	North America, Europe, Asia	1	0.78
Plantago ispaghula	Asia	1	0.4	*Hibiscus sabdariffa*	Africa	1	0.78
Psyllium husk	Europe	1	0.4	*Vaccinium myrtillus*	Europe	3	2.34
Pygeum africanum	Africa	1	0.4	*Sambucus nigra*	Africa, Asia and Europe	6	4.69
Ribes	Europe	1	0.4	*Commiphora abyssinica*	Africa	2	1.56
Rumex crispus	Europe	1	0.4	*Zingiber officinale*	Asia	3	2.34
Ruscus aculeatus	Europe	1	0.4	*Ziziphus spinosa*	Asia	2	1.56
Sacharomyces cerevisiae	N/A	1	0.4	*Angelica sinensis*	Asia	2	1.56
Salix alba	Europe	1	0.4	*Verbascum thapsus*	South America	2	1.56
Salvia	Central America	1	0.4	*Valeriana edulis*	Asia and Europe	5	3.91
Sambucus	Mexico	1	0.4	*Passiflora edulis*	South America	3	2.34

Table 1. *Cont.*

Herbal Medicines	Origin	Sanitary Registries	(%) Sanitary Registries	Herbal Remedies (Continuation)	Origin	Sanitary Registries	(%) Sanitary Registries
Senna alexandrina	Africa	1	0.4	*Agastache mexicana*	Mexico and South America	9	7.03
Symphytum officinale L.	Europe	1	0.4	*Morinda citrifolia*	Asia	1	0.78
Tenacetum parthenium	Europe	1	0.4	*Plantago lanceolata*	Asia and Europe	1	0.78
Thymus	Europe	1	0.4	*Trigonella foenum*	Asia	1	0.78
Uncaria tomentosa	South America	1	0.4	*Selaginella lepidophylla*	North America	2	1.56
Vinca minor	Europe	1	0.4	*Equisetum*	Mexico and North America	3	2.34
Vitex agnus castus	Europe	1	0.4	*Salix taxifolia*	Mexico	1	0.78
Zingiber officinale	Asia	1	0.4	*Ibervillea sonorae*	Central and North America	1	0.78
Curcuma longa L.	Asia	1	0.4	*Eysenhardita polystachya*	Central and North America	1	0.78
Herbal remedies	**Origin**	**Sanitary registries**	**(%) sanitary registries**	*Amphipterygium adstringens*	Mexico	7	5.47
Arctium lappa	Asia and Europe	1	0.78	*Hintonia latiflora*	Mexico	2	1.56
Rumex acetosella	Asia and Europe	1	0.78	*Conyza filaginoides*	Mexico and South America	3	2.34
Ulmus rubra	North America	1	0.78	*Coutarea latiflora*	Mexico	1	0.78
Trigonella foenum	Asia	1	0.78	*Eryngium heterophyllum*	Mexico	1	0.78
Cecropia obtusifolia	Mexico and South America	2	1.56	*Taraxacum officinale*	China	1	0.78
Opuntia	America	4	3.13	*Ocimum basilicum*	Asia	1	0.78
Ginkgo biloba	China	1	0.78	*Allium sativum*	Asia	3	2.34
Echinacea	North America	5	3.91	*Petroselinum crispum*	Asia and Europe	2	1.56
Marrubium vulgare	Africa, Asia and Europe	1	0.78	*Temstroemia pringlei*	Mexico and North America	1	0.78
Glycyrrhiza glabra	Asia and Europe	1	0.78	*Momordica charantia*	Asia	2	1.56
Castela texana	North America	1	0.78	*Juglans regia*	Asia and Europe	1	0.78

4.5. Native Plants from Mexico Used in Herbal Products

The most popular medicinal plants used for herbal medicines are native plants from other regions of the world, mostly Europe and Asia. Out of 241 sanitary registries, only 3 plants are native to Mexico, according to COFEPRIS [8]. On the contrary, for herbal

remedies, it was observed that of 129 sanitary registries, at least 21 plants are native Mexican.

The review of popular medicinal plants of herbal products elicited 24 native plants from Mexico: *Persea gratissima*, *Phaseolus vulgaris*, *Sambucus, Cecropia obtusifolia*, *Smilax cordifolia*, *Tilia Mexicana*, *Tecoma stans*, *Turnera diffusa*, *Jacobinia spicigera*, *Ipomoea purga*, *Artemisa mexicana*, *Capsicum annum*, *Guazuma ulmifolia*, *Crescentia alata*, *Sambucus mexicana*, *Equisetum*, *Salix taxifolia*, *Amphipterygium adstringens*, *Hintonia latiflora*, *Conyza filaginoides*, *Coutarea latiflora*, *Eryngium heterophyllum*, *Ternstroemia pringlei*, and *Agastache mexicana*.

The data reveal that the field of study on medicinal plants in our country with native species is not sufficiently explored, given the great floristic diversity in Mexico. The above table is indicative of an area with great potential for the study of these species, where various strategies are used, such as the study of chemical, biological, and genetic characterization of these resources, even applying "omic" tools, a current trend [32].

4.6. General Characteristics of Mainly Native Plants from Mexico Used in Herbal Products

This review presents information collected from scientific reports on the biological properties of plants with the highest number of registers for herbal medicine and herbal remedies (Tables 2 and 3) *Persea grattisima, Phaseolus vulgaris, Sambucus*, *Agastache Mexicana*, *Amphipterygium adstringens, and Turnera diffusa* and their potential therapeutic applications. The bioactivities and mechanism of action reported in the literature on the plants are described below, considering that regulation did not require evidence for the registration of these products.

Table 2. Native plants used in herbal medicines with mainly biological activity and number of registers.

Herbal Medicine	Status	Biological Activity	Registers	Reference
Persea gratissima	Native	Antiartritic,	1	[33]
Phaseolus vulgaris	Native	Hypoglycemic, Antihyperlipidemic	1	[34]
Sambucus	Native	Respiratory diseases	1	[35]

Table 3. Native plants used in herbal remedies with mainly biological activity and number of registers.

Herbal Remedies	Status	Biological Activity	Registers	Reference
Cecropia obtusifolia	Native	Hypoglycemic	2	[36]
Smilax cordifolia	Native	Antihyperlipidemic, anti-inflamatory	2	[37]
Tilia mexicana	Native	Sedative, anxiolytic	1	[38]
Tecoma stans	Native	Digestive functions	3	[39]
Turnera diffusa	Native	Aphrodisiacs	4	[40]
Jacobinia spicigera	Native	Respiratory diseases	1	[41]
Ipomea purga	Native	Heart disease	1	[42]
Artemisa mexicana	Native	Digestive functions	1	[43]
Capsicum annum	Native	Digestive functions	2	[44]
Guazina ulmifolia	Native	Digestive functions	1	[45]
Crescentia alata	Native	Respiratory diseases	1	[46]
Sambucus mexicana	Native	Respiratory diseases	1	[47]
Equisetum	Native	Nefropatia	3	[48]
Salix taxifolia	Native	Nefropatia	1	[49]
Amphipterygium adstringens	Native	Digestive functions	7	[50]
Hintonia latiflora	Native	Digestive functions	2	[51]
Conyza filaginoides	Native	Digestive functions	3	[52]
Coutarea latiflora	Native	Digestive functions	1	[53]
Eryngium heterophyllum	Native	Antihyperlipidemic	1	[54]
Ternstroemia pringlei	Native	Insomnia	1	[55]
Agastache mexicana	Native	Anti-inflamatory	9	[56]

4.6.1. *Persea grattisima* (Avocado Fruit)

Persea grattisima and *Persea americana* unsaponifiable oil, in combination with soybean (33.3:66.6), is prescribed for osteoarthritis. The oil enhances the synthesis of collagen and proteoglycan and decreases the synthesis of fibronectin. Another mechanism of action is the inhibition of the release and activity of metalloproteinases and proinflammatory cytokines such as IL-1, IL-8, and PGE2 [57–59]. Additionally, in vitro studies have shown that the oil mixture stimulates aggrecan and matrix component synthesis, reduces catabolic and proinflammatory mediator production, and appears to prevent the osteoarthritic osteoblast-induced inhibition of matrix molecule production, suggesting that this compound may promote osteoarthritis cartilage repair by acting on subchondral bone osteoblasts [57].

The clinical data suggest that unsaponifiable oil from avocado and soybean can efficiently supplement long-term treatments of knee and hip osteoarthritis [57,59,60].

4.6.2. *Phaseolus vulgaris*

The seed of this plant (beans) has been investigated for several bioactivities. One of them is the inhibitor of alpha-amylase, which has anti-obesity effects, as well as the ability for reducing post-prandial peaks from blood glucose in clinical trials [38] and facilitates digestion and prevents constipation [61,62]. Otherwise, inhibition in vivo of maltase and saccharase was reported in rats [63].

4.6.3. *Sambucus*

Sambucus nigra flower (elderflower) and fruit (elderberry) extract, which is prescribed for flu symptoms, have demonstrated ancestral medicinal properties even for respiratory viral pathogens, such as influenza and cold. The elderflowers are composed of a diversity of bioactive molecules such as free aglycones, flavonol glycosides, phenolic compounds, sterols, triterpenes, free fatty acids, alkanes, and tannins. Antiviral activity has been tested against dengue virus serotype-2, influenza, herpes simplex virus type 1, parainfluenza, influenza, and respiratory syncytial virus. However, reports of clinical trials demonstrating the efficacy of elderflower extract do not exist, even though four trials exist that use elderberry extracts [64–66].

4.6.4. *Agastache mexicana*

A. mexicana is a Mexican medicinal plant commonly known as "toronjil morado". It is an endemic plant in Mexico that is prepared as an infusion or decoction, also maceration in ethanol of aerial parts. The biological activity is used for treating nervous system issues, insomnia, cardiovascular disorders, and gastrointestinal diseases [67–69]. The major compounds in this medicinal specie are monoterpenes such as limonene and pulegone [70]. The anti-inflammatory activity of limonene has been demonstrated, while the nociceptive behavior of pulegone has been reported [71,72]. Recent scientific evidence showed that the compounds present in the medicinal plant *A. mexicana* can reduce symptoms such as pain and inflammation in gastrointestinal disorders, implying the potential use of the monoterpenes present in the plant for therapeutic purposes and treatment of abdominal pain, colitis, and ulcers [69].

4.6.5. *Amphipterygium adstringens*

Commonly known as "Cuachalalate", it is a dioecious tree endemic to Mexican tropical dry forests [73]. The biomedical properties have been extensively studied, including astringent and hypocholesterolemic properties, as well as their effectiveness for treating cancer and gastritis. The bark has traditionally been used by healers to treat gastritis, gastric ulcers, gastrointestinal cancer, colic, fever, and also tooth pain. The phytochemical constituents of Cuachalalate bark are categorized into two main groups: triterpenes and long-chain phenolic compounds [74]. In particular, *A. adstringens* have a high commercial demand in Mexico [75]; 57.5 tons of bark per year are estimated in south-central Mexico [76].

In a recent report, we demonstrated that the extract of *A. adstringens* ("cuachalalate") has substantial potential for the treatment of inflammatory colitis [77].

4.6.6. *Turnera diffusa*

Turnera diffusa, commonly known "damiana", is a shrub that grows in arid and semi-arid regions of South America, Mexico, the United States, and the West Indies. Several properties have been attributed to this plant. Usually, the leaves of the plant are used to prepare a decoction [78,79]. Phytochemical investigations have been conducted to isolate and identify some components present in the plant, among which are flavonoids, sesquiterpenes, triterpenes, polyterpenes, fatty acids, and xanthine-derived sugars [40,80]. In a recent study, methanolic extract of *T. diffusa* was demonstrated to have an antidiabetic effect of Teuhetenone A in a diabetic mice model [81].

5. Challenges and Future Perspectives

The use of medicinal plants is associated with a longstanding history of evolution and development across the centuries. Current research work in our country is based on the specific study of molecules with pharmacological action, isolation, and structural studies to develop or define new properties. The limited study of the molecules that generate a pharmacological effect based on their pharmacokinetics and pharmacodynamics does not contribute novel approaches that focus on the analysis of new pharmacological properties and, in turn, biological and cellular activities, with the objective of expanding the potential methods for treatment of human diseases, which increasingly require greater knowledge, even at the molecular level [82]. Thus, we find that the study and use of the genetic resources of medicinal plants are very limited. The approach with which the genome of medicinal plants should be evaluated must use state-of-the-art technologies and a holistic approach, in addition to integrating the data of the omics sciences to address research questions. Sciences such as genomics, proteomics, transcriptomics, metabolomics, synthetic biology, and system biology, among others, must be combined to offer concrete approaches to the rational medical use of medicinal plants. With these studies focused on the use of plant resources of medicinal plants, we may identify a relationship between genetic resources, qualitative and quantitative chemical quality, and the efficacy of drugs and/or remedies.

One of the main concerns associated with the use and exploitation of native plants that have a specific medicinal use is the depredation and potential impact on the environment by overexploiting a native resource, which, if not used carefully, can be lost. However, the study of genetic resources gives rise to the generation of gene libraries, wherein we have certainty of the metabolic route for the synthesis of metabolites and/or biological products of pharmaceutical interest. Specifically, active ingredient biosynthesis genes can be studied, their evolutionary history, and their domestication process analyzed, in addition to identifying genes that respond to environmental stress to help improve their resistance and capacity. The sustainable use of medicinal plants can be favored during the systematic analysis of gene functions, functional genomics analysis, and the search for model plants. All this information could generate an area termed "functional herbal genomics", which contributes to solid research platforms such as synthetic biology and geo-herbal research, whose main purpose is to ensure the supply of medicinal plants and their bioactive compounds in the future [83].

Despite the given context, the powerful capacity and perspectives of medicinal plants continue to be underestimated, and their ability to resolve practical concerns in their use and exploitation remains to be investigated.

It is not yet certain how the genome of medicinal plants could be used to transform and generate efficient varieties. One of the main approaches where the process of study and investigation can be initiated is the identification of potential model medicinal plants, which would allow us to obtain complete metabolic patterns and modification of the

routes, in turn, generating greater concentrations of specific metabolites with interesting pharmacological properties.

Another of the great challenges in the study of the genome of medicinal plants is the vast generation of genomic data to study. While advances in sequencing technologies and the assembly of sequences have been very important in recent years, there remain challenges to be overcome, such as high repetitiveness, high content of scaffolds or super scaffolds, and other concerns associated with the correct assembly of complete chromosomes.

However, the challenges and perspectives in the study of medicinal plants are increasing, although several difficulties have been overcome. By continuing to bet on the study of the basic science of genetic resources of herbal plants, successes will soon be reaped, such as new therapies based on herbal medicine, which are as effective as any pharmacochemical.

6. Conclusions

In conclusion, from the sanitary registries of herbal products, including herbal medicine and herbal remedies in Mexico during the 2001–2020 period, it has been inferred that most pharmaceutical laboratories that produce these products are Mexican. Nevertheless, the minority of the plants used for their manufacturing are from Mexican native plants. On the other hand, limited pharmaceutical technology has been evidenced since capsules are the most frequent pharmaceutical form. Further, the highest number of therapeutic indications were disorders and diseases that seem to be focused on non-common morbidity causes (such as weight loss and improvement of physical/mental performance) rather than mortality causes. Regulation of herbal products in Mexico, while beneficial, carries great room for improvement to ensure efficacy and safety in treatments. The potential use of resources from medicinal plants is evident. However, there is still a long way to go. Studying medicinal plants from a holistic approach can be the first step toward finding future drugs, chemical structures, genetic resources, new metabolic pathways, bioactive compounds, and novel uses of underutilized resources.

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