Medicinal and Aromatic Plants of the World 6

Akos Máthé *Editor*

Medicinal and Aromatic Plants of North America

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Volume 6

Series Editor
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Medicinal and Aromatic Plants (MAPs) have been utilized in various forms since the earliest days of mankind. They have maintained their traditional basic curative role even in our modern societies. Apart from their traditional culinary and food industry uses, MAPs are intensively consumed as food supplements (food additives) and in animal husbandry, where feed additives are used to replace synthetic chemicals and production-increasing hormones. Importantly medicinal plants and their chemical ingredients can serve as starting and/or model materials for pharmaceutical research and medicine production. Current areas of utilization constitute powerful drivers for the exploitation of these natural resources. Today's demands, coupled with the already rather limited availability and potential exhaustion of these natural resources, make it necessary to take stock both of them and enrich our knowledge regarding research and development, production, trade and utilization, and especially from the viewpoint of sustainability. The series Medicinal and Aromatic Plants of the World is aimed to look carefully at our present knowledge of this vast interdisciplinary domain, on a global scale. In the era of global climatic change, the series is expected to make an important contribution to the better knowledge and understanding of MAPs. The Editor of the series is indebted for all of the support and encouragement received in the course of international collaborations started with his ISHS involvement, in 1977. Special thanks are due to Professor D. Fritz, Germany for making it possible. The encouragement and assistance of Springer Editor, Mrs. Melanie van Overbeek, has been essential in realizing this challenging book project. Thanks are due to the publisher - Springer Science+Business Media, The Netherlands - for supporting this global collaboration in the domain of medicinal and aromatic plants. We sincerely hope this book series can contribute and give further impetus to the exploration and utilization of our mutual global, natural treasure of medicinal and aromatic plants.
Budapest, Prof. Dr. Ákos Máthé.

More information about this series at http://www.springer.com/series/11192

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Preface and Dedication

The present volume is part of the series Medicinal and Aromatic Plants of the World. Similar to the previous five volumes, the contributing authors are well-known personalities from their relevant scientific fields in different domains of the medicinal plant profession.

The aim of the volume is to introduce the wealth and diversity of Medicinal and Aromatic Plants (MAPs) on the North American continent. The authors would like to offer the readers an insight into the broad spectrum of medicinal and aromatic plants on this huge, diverse, as well as rich continent: from traditional uses to the prospective production and utilization. This aim is mainly served by a general introductory chapter, but specifically also other chapters reveal interesting aspects of the relevant medicinal plant species.

The topics have been chosen, with preference, in such a way as to present true American success stories on medicinal plants, e.g., American cranberry, American ginseng (*Panax quinquefolius)*, Taxol *(Taxus brevifolia)*. To date, these are considered as classical examples of successful medicinal plant R&D and utilization. Wherever possible, these reviews will encompass the past, present, and future aspects of these commodities.

As demonstrated by this book, the USA, at present, is an excellent example to illustrate the wide-ranging activities that are needed to produce and use MAPs in a sustainable way. In this activity, special attention is paid to the conservation of their genetic resources.

The North American continent, more specifically the USA, is home to several important initiatives aimed at educating the herbal and dietary supplement industry about such important issues as ingredient and product adulteration, botanical raw material sourcing and sustainability, regenerative and sustainable agriculture, botany, ethnobotany, ethnobiology, horticulture, pharmacognosy, wild harvesting, herbal medicine, etc.

In a historical perspective, a separate chapter in the book deals with the impact of legislation (Dietary Supplement Health and Education Act of 1994), as well as issues related to the sustainable supply/conservation of good-quality botanicals

(Good Agricultural and Collection Practice – GACP) to be used with safety and with efficacy.

This volume is dedicated to the memory of the late botanist **Professor Dr. James (Jim) Duke**, who regretfully could not contribute to this volume any more. His memory should, however, be commemorated not only by this volume but also by the dozens of other milestone comprehensive volumes and scientific volumes on MAPs.

On a more personal note, the editor of the volume still recalls the memory of the friendly, hilarious musician personality of Jim Duke, the "herbal cowboy," whom he had the opportunity to meet at USDA ARS, in Beltsville, during his Fulbright scholarship, in 1984. Jim has written some 400 herbs-related poems and composed a vinyl record-full of "blue grass songs" that were not only written but also performed by him personally. A really unforgettable personal touch for the visiting young Hungarian Fulbright scholar, at USDA ARS, in Beltsville, who was trying to get orientated in the matters of horticultural research in America of the 1980s.

As rendered possible by fate, the Editor of this volume has had the opportunity to spend another half-year in the USA, teaching a course on the "production and biology of MAPs," at UMASS, Amherst. Another excellent chance to get acquainted, to study the North American traditions and system of medicinal and aromatic plant production and utilization.

There seem to be nearly endless approaches for a book to deal with the Medicinal and Aromatic Plants of North America. I am convinced, however, that the knowledge and experience of the authors compiled here has resulted in a useful as well as interesting volume that, regarding its contents, is sufficiently comprehensive and varied to serve as a good resource of orientation on Medicinal and Aromatic Plants of North America.

Finally, editor expresses special thanks to Prof. Dr. Lyle Craker, UMASS, Amherst and Josef Brinckmann, PhD, research fellow at Traditional Medicinals, Inc., Sebastopol, CA, for their support and critically reading relevant parts of the manuscript.

Mosonmagyaróvar, Hungary Ákos Máthé
January 6, 2020

Contents

Chapter 1
Introduction to Medicinal and Aromatic Plants in North America

Ákos Máthé

Abstract Native American peoples developed a sophisticated "plant-based medical system" in the course of millennia before the European conquest of America. Despite the significant differences between the systems developed by the various native groups, there were also many broad similarities. Out of the approximately 28,000 species of plants in North America, native Americans used about 2500 medicinally.

Out of the thirty-six areas that qualify as biodiversity hotspots, for North America and Central America, only three regions qualify: the California Floristic Province, Madrean pine-oak woodlands, and Mesoamerica.

Recently, also the North American Coastal Plain (NACP) has been identified as a global hotspot: this finding they have based on its similarity with the classic definition of a region.

The Flora of North America North of Mexico (FNA), is conceived as a multivolume work describing the native plants of North America, in 30 volumes. 17 volumes of the Flora are already available online.

Germplasm conservation in the United States is not new. Realizing the importance of genetic diversity, the USDA has been collecting and preserving germplasm since the late 1800s. To date, the National Genetic Resources Program (NGRP) of USDA acquires, characterizes, conserves, documents, and distributes to scientists germplasm of all life forms important for food and agricultural production.

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The U.S. Department of Agriculture's Foreign Agricultural Service maintains statistics on imported herbs and spices but there is no systematic process for measuring wild-harvested (a.k.a. wildcrafted) or commercially cultivated herbs used in the medicinal plant market. In view of the increasingly strict quality requirements, the American Herbal Products Association (AHPA) published its Good Agricultural and Collection Practices (GACPs) and Good Manufacturing Practices (GMPs) for botanical materials. In the US, GACP implementation is mandatory only for botanical drug active ingredients: voluntary for botanical dietary supplement ingredients. As the U.S. Food and Drug Administration (FDA) has not yet established its own GACPs for botanical drugs, the agency specifically accepts GACP compliance according to guidelines published by the European Medicines Agency (EMA) and the World Health Organization (WHO).

In the US and Canada, pharmaceutical drugs are subject to strict regulations, like in most countries. Their availability is similarly restricted as either prescription drug products (Rx) or nonprescription over-the-counter (OTC) drug products. The regulation of medicinal and aromatic plant (MAP) production, trade and use in North America is the result of the influence of a multitude of contributing "actors" (governmental agencies, intergovernmental organizations, public institutions, standard-setting organizations, and other bodies). Much progress has been made since the 1800s, when the patent medicines (proprietary medicines made and marketed under a patent and available without prescription) first became popular. In the lack of Federal regulations for these products prior to the passage of the Pure Food and Drug Act of 1906 and subsequent United States Federal Food, Drug, and Cosmetic Act of 1938, consumers had no means to distinguish between false and valid claims. Many of these were of plant origin and often had "secret formulations". There is good reason to believe in the truth of Professor Varro Tyler's forecast saying: "Looking back, it is obvious that a great deal of progress has already been made. We now look to the future with eager anticipation and great expectations."

Keywords North America · Canada · Medicinal and Aromatic Plants · Biodiversity hotspots · Flora · Natural conservation · Official and public participants of legal regulation

1.1 Introduction

The present volume will deal with Medicinal and Aromatic Plants of Northern America. To allow for the fine tuning of the geographic scopes, in the present volume we set the boarder lines of North America to comprise the territory of the non-tropical area of the United States of America and Canada. As such, the volume will deal with MAPs in the conterminous 48 states of USA on the Canada, bordered on the east by the Atlantic Ocean, on the south by the Gulf of Mexico and Mexico, and on the west by the Pacific Ocean. The total area is ca. 9,809,630 square kilometers.

In the North, Canada is composed of ten provinces and three territories that extend from the Atlantic to the Pacific and northward into the Arctic Ocean, covering 9.98 million square kilometers (3.85 million square miles), making Canada the world's second-largest country by total area.

The US is home to many natural resources including MAPs.

In this context we would like to refer to the fact that the notion of Medicinal and Aromatic Plants (MAPs) seems to be fundamentally vaguely defined to denote either a group of plants that due to their biologically active substances are used to cure, ease or prevent diseases (Hoppe 2009) and/or plants that are distinguished due to the intensive, plant-specific fragrance (scent) of their leaves and flowers. This category is used only seldom in relevant surveys on natural resources and remarkably, Medicinal and Aromatic Plants generally do not qualify among the first ten most valuable resources, although since times immemorial, herbs and their use have thrived on this continent. Frequently used synonyms for MAPs are: herbs, botanicals, crude drugs, etc. Also, Essential Oil and Aromatic Plants is a term frequently used as a synonym to denote plants that contain volatile oils: aroma plants, however, distinguish themselves by their combined, mostly pleasant, scent and taste.

Similarly to the versatility of their natural occurrence and ecological roles (defense against insects, fungi, diseases and herbivorous animals) and due to their contents of phytochemicals with potential or established biological activity, the use of MAPs by man is also most versatile: herbal medicine, food-, feed additives, cosmetics, etc. (see: Máthé 2015).

In view of above-mentioned, the aim of this chapter is not to offer introduction to the vast scenery of MAPs utilization on the equally huge North American continent. It is meant to serve *quasy* as an "apetizer" demonstrating the nearly unlimited resources and values hidden in this group of economic plants on this large continent. All this will be presented, in a *quasi* historical perspective, so that in view of the past, present and the nearly unlimited prospective opportunities standing in front of MAPs can be projected It is our hope that the believed and/or legitimate shortcomings can remediated in the prospective volumes of the MAPW series.

1.2 Biodiversity Hotspots in North America

Biodiversity hotspots are biogeographic regions that are both biologically rich and highly threatened with destruction from urbanization, development, pollution, and diseases. For a region to be classified as a biodiversity hotspot, it must have at least 1500 vascular plants strictly endemic to the habitat and must have at most 30% of its original natural vegetation (Myers et al. 2000).

Biodiversity hotspots are not uniformly distributed on Earth. Out of the thirty-six areas that qualify as biodiversity hotspots, for North America and Central America, only three regions qualify: the **California Floristic Province**, **Madrean pine-oak woodlands**, and **Mesoamerica** (Molly 2018). These regions support nearly 60% of world's mammal, plant, amphibian, reptile, and bird species, a majority of which are endemic to the specific hotspots (Fig. 1.1) a great deal of conservation is required to preserve the remaining land of these species. Regarding the fact that Mesoamerica's span is mostly Central America, this hot-spot shall not be discussed here among the North American hot-spots.

Recently, however, Noss et al. (2015) have identified also the **North American Coastal Plain** (NACP) as a global hotspot: this finding they have based on its similarity with the classic definition of a region: i.e. >1500 endemic plant species

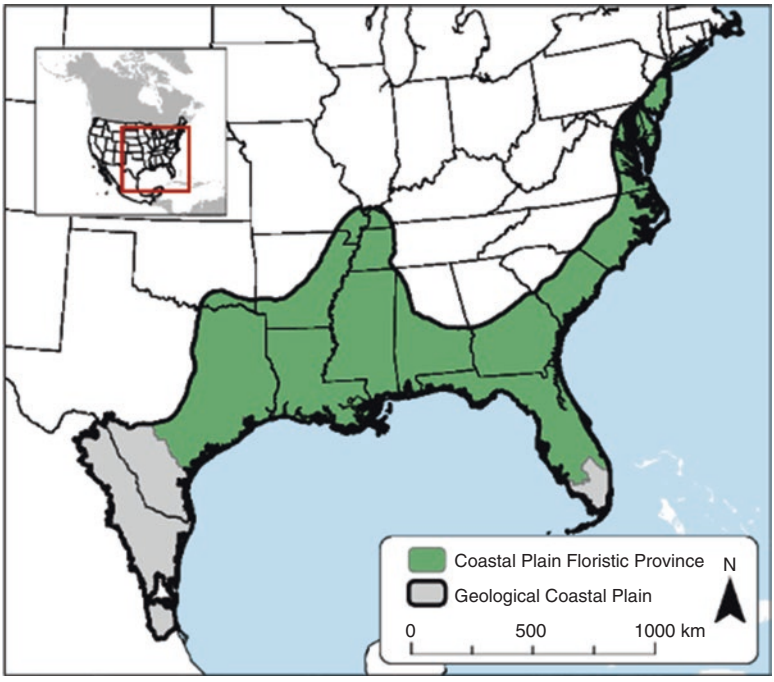

Fig. 1.1 The Geological Coastal Plain (GCP) and the Coastal Plain Floristic Province (CPFP). The CPFP is contained within the GCP. (Noss et al. 2015)

and > 70% habitat loss. In their proposal Noss et al. (2015) refer to their "suspicion" according to which there are systematic biases and misconceptions, in addition to missing information, that obscure the existence of similarly biologically significant regions world-wide.

1.2.1 California Floristic Province

The California Floristic Province is located along North America's Pacific coast. It is a zone of Mediterranean-type climate and is characterized by hot, dry summers and cool, wet winters (Molly 2018).

The California Floristic Province is home to 3488 native plant species, 2100 of which are endemic to the region. The region contains a wide variety of ecosystems, including sagebrush steppe, prickly pear shrubland, coastal sage scrub, chaparral, juniper-pine woodland, upper montane-subalpine forest, alpine forest, riparian forest, cypress forests, mixed evergreen forests, Douglas fir forests, sequoia forests, redwood forests, coastal dunes and salt marshes. Today, a quarter of the original vegetation has remained in a more or less pristine condition. The hotspot is home to the endangered giant sequoia *(Sequoiadendron giganteum*), the planet's largest living organism and its taller but less massive relative, the endangered coastal redwood (*Sequoia sempervirens*).

Located in the most populated and fastest growing regions of the US, the biodiversity of this region has been threatened by urbanization, pollution, agriculture, mining, logging, and even intentional fires. According to approximations, due to land reclamation, the salt and freshwater ecosystems have declined by 90%. As only 25% of the hotspot holds its pristine nature, great deals of conservation efforts are needed to protect the hotspot (Molly 2018).

1.2.2 Madrean Pine-oak Woodlands

This biodiversity hot-spot is located in the higher elevations of the mountain ranges of Mexico, as well as the US states of Arizona, New Mexico, and Texas. It is regarded as – probably - the world's richest and most endangered terrestrial ecosystem.

It comprises different habitats including tropical, subtropical, dry shrublands, and grasslands with 5300 flowering plants: 2000 species being unique to Madrean Sky Islands. The consistent pine, oak, Douglas fir, and fir species coupled with varying orientation of slopes, soil types, climate and geologic history give the hotspot its cohesive character.

Among the several threats to the Pine-Oak woodlands, illegal logging poses the greatest threats. Non-wood products including the vascular epiphyte are extracted and a variety of mushroom species found in the pine-oak forests are collected for

culinary purposes. Intentional fires in favor of agricultural activity have largely altered habitats throughout the woodland forests .

1.2.3 North American Coastal Plain (NACP)

Recently, Noss et al. (2015) have identified also the North American Coastal Plain (NACP) as a new global hotspot. Their assumption / proposal they have based on similarities 6 compliances with the classic definition of a region with >1500 endemic plant species and > 70% habitat loss.

Based on their case study, they claim that this region has been bypassed in prior designations due to misconceptions and myths about its ecology and history. These fallacies include: (1) young age of the NACP, climatic instability over time and submergence during high sea-level stands; (2) climatic and environmental homogeneity; (3) closed forest as the climax vegetation; and (4) fire regimes that are mostly anthropogenic. They have demonstrated that the NACP is older and more climatically stable than usually assumed, spatially heterogeneous and extremely rich in species and endemics for its range of latitude, especially within pine savannas and other mostly herbaceous and fire- dependent communities.

Noss et al. (2015) do not only attempt to improve the understanding of this region and to promote its recognition as a hotspot. With this effort they also promote the appreciation and improved conservation of ecologically and evolutionarily similar regions globally.

1.3 Diversity of Plants in North America (Biomes)

The North American continent, makes up about 4.8% of the total surface area of the planet. This continent alone has 15 broad, level I ecological regions; 50 level II ecological regions intended to provide a more detailed description of the large ecological areas nested within the level I regions; and 182 Level III ecoregions, which are smaller ecological areas nested within level II regions (US Environmental Protection Agency Protection n.d.). A map of major terrestrial ecoregions is contained in Fig. 1.2.

Ecological hierarchy at this scale provides a context for revealing global and/or intercontinental patterns. Level I. **ecological regions** are: Arctic Cordillera, Tundra, Taiga, Hudson Plains, Northern Forests, Northwestern Forested Mountains, Marine West Coast Forests, Eastern Temperate Forests, Great Plains, North American Deserts, Mediterranean California, Southern Semi-Arid Highlands, Temperate Sierras, Tropical Dry Forests and Tropical Humid Forests.

In terms of biomes, from the overall 15 terrestrial and 12 aquatic biomes of the world, North America is frequently, broadly categorized into the following **six major biomes**: the Tundra biome, Coniferous forest biome, Prairie biome, Deciduous forest biome, Desert biome, and the Tropical rainforest biome.

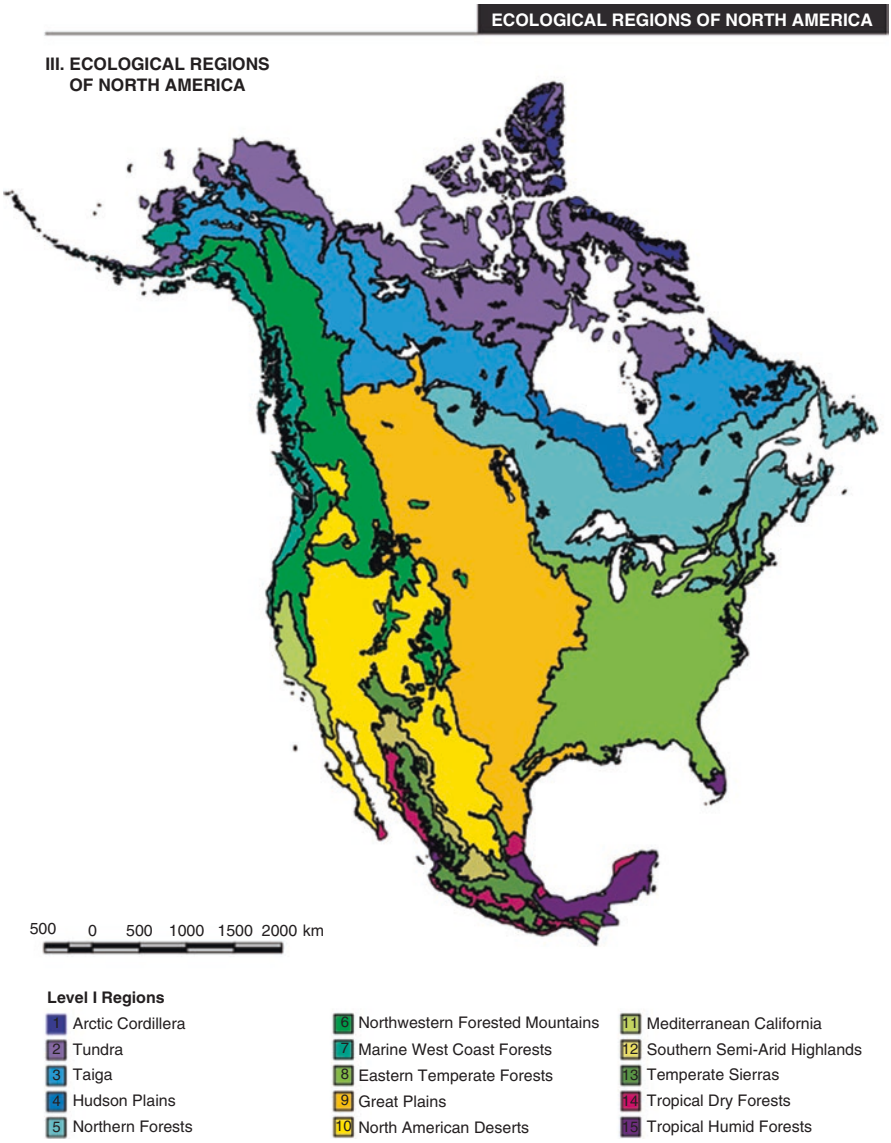

Fig. 1.2 III. Ecological regions of North America. (Source: CEC Secretariat 1997)

As a result of continental drift, the United States is located currently almost exclusively in the North temperate zone (Mauseth 2014) and receives much of its weather from the Pacific and Arctic Oceans in winter, and from the Pacific Ocean and the tropical Atlantic Ocean in summer.

Tundra Biome Typically, it is characterized by harsh climatic conditions, permafrost (frozen soil) and as a consequence, the lack of evergreen vegetation. Despite

the climatic conditions that are unsuitable for human habitation, several plants and animals have adapted themselves to the harsh climate prevailing in this region. The plant species found in the Tundra biome include various species of shrubs, mosses, grasses, and lichens.

Coniferous Forest Biome A North American biome that is typically characterized by a wide variety of coniferous trees, such as pine, fir, and spruce. The average temperature in this region in winter is as low as 14 °F, while the average rainfall in this region ranges between 14–29.5 inches. A range of herbivorous animals inhabit this region, feeding on the leaves of coniferous trees that grow here in abundance.

Prairie Biome Is also known as the North American prairie. This biome is predominantly characterized by a wide variety of herbaceous plants and grasses. Spanning an area of 1.4 million sq. mi, these grasslands generally receive annual precipitation between 12.6–21.7 inches. The plant species found in this region include big bluestem grass, blue grama grass, buffalo grass, etc. The ethnobotanist Kindscher (1992) documents the medicinal use of 203 native prairie plants by the Plains Indians.

Deciduous Forest Biome The deciduous forest biome is found in the eastern region of North America. On an average, this region experiences an annual rainfall ranging between 30–60 inches. The average annual temperature in this region is around 50 °F. The plant species native to the North American deciduous biome include the American beech, white birch, white oak, etc. The medicinal species common to this biome include wood sorrel (*Oxalis montana*), but also many European to Eurasian species, that long ago escaped and naturalized in North America includingdandelion (*Taraxacum officinale*), stinging nettle (*Urtica dioica*), chickweed (*Stellaria media*), and broadleaf plantain (*Plantago major*),, etc. (Wisniewski 2017).

Desert Biome The desert biome, in North America, comprises deserts such as the Sonoran Desert of southern Arizona and the Mojave Desert of California. The region is dominated by drought-resistant species, such as the saguaro (*Carnegiea gigantean*) and Joshua tree (*Yucca brevifolia*) or *Agave* species, *Amaranthus* species, *Bowlesia* species, devil's claw (*Proboscidea* species, not to be confused with the native African devil's claw of *Harpagophytum* species), blue dlder (*Sambucus cerulea*) and Mexican elder (*Sambucus mexicana*), etc.

Tropical Rainforest Biome vs. Temperate Rain Forests Although in most discussions, the Tropical rain forest biome is usually mentioned as a component of North American biomes, we also use this term for the sake of completeness, it must be emphasized that in our concept, North America is meant to denote and encompass mainly the territory of both Canada and the United States of America. (The territories north of the Darien Gap, will be discussed in a separate volume, in relation to Central America.).

Temperate rainforests are coniferous or broadleaf forests that occur in the temperate zone and receive heavy rainfall. Temperate rainforests only occur in a few regions around the world, Most of these occur in oceanic moist climates: the Pacific temperate rain forests in Western North America (Southeastern Alaska to Central California). They also comprise the the Appalachian temperate rainforest of the Eastern U.S. The latter region is home to 125 plant species for medicinal use (Krochmal 1968), including black cohosh (*Actaea racemosa*), blue cohosh (*Caulophyllum thalictroides*), goldenseal (*Hydrastis canadensis*), North American wild yam (*Dioscorea villosa*), purple angelica (*Angelica atropurpurea*), and sassafras (*Sassafras albidum*), etc.

1.4 Flora of North America (FNA) vs. New Naturalized Species

The Flora of North America North of Mexico (usually referred to as FNA, is a multivolume work describing the native plants of North America. 17 volumes of the Flora are already available online (Flora of North America Editorial Committee 1993). It is expected to fill 30 volumes when completed and will be the first work to treat all of the known flora north of Mexico.

1.5 Natural Conservation of MAPS vs. Diversity Loss

According to Moerman (1996) native Americans used 2564 of 21,641 vascular species, or 11.8% of the available flora for medicinal purposes (Moerman 1996).

In an editorial under the title "A Census of Botanical Risk" of the New York Times. April 12, 1998), exactly 10 years after the Chiang Mai Declaration (1988), Johnston (1998) called attention to the serious losses in biodiversity (including MAPs). He stated that at least one out of every eight known plant species on Earth was either threatened with extinction or nearly extinct. In the United States, that probably has the planet's best-studied flora, about 29% of 16,000 species were at risk.

As a remarkable interpretation of these figures David G. I. Kingston (2011) explained "Plants have historically provided some of the most important drugs that we have," e.g.: morphine, aspirin, and quinine, as well as a number of less common drugs such as anti-cancer medications derived from the periwinkle, etc. "We've screened about 50,000 plant species so far, and gotten about 50 drugs," Kingston said, "so that's about one per thousand." If the same ratio of 1:1000 holds, the loss of 34,000 species could well doom development of 34 pharmaceuticals.

Nearly at the same time, in 1997, the International Union for Conservation of Nature (IUCN), in collaboration with the Smithsonian, the World Wildlife Fund (WWF) and 10 other government and independent research and conservation groups in a half-dozen countries compiled a 862-page report, titled "1997 IUCN Red List of Threatened Plants" (Walter et al. 1998).

> To be classified as threatened, a species must have reached the point at which there are fewer than 10,000 individuals worldwide, or fewer than 100 locations in which it is found. Comparing the latest census against decades of field records and combined collections totaling 20 million specimens, experts found a pace of species decline far above the historic extinction rate. The study included only vascular plants, those with water and nutrient-conducting tissues. Algae, lichens, fungi and the like were not studied.

Concerning the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES), several North American MAPs were listed in CITES Appendix II including wild American ginseng roots (*Panax quinquefolius* L., Araliaceae) in 1975, candelilla (*Euphorbia antisyphilitica* Zucc., Euphorbiaceae) in 1975, goldenseal (*Hydrastis canadensis* L., Ranunculaceae) in 1997, and guaicum (*Guaiacum sanctum* L., Zygophyllaceae) in 1975.

As an example, Baum et al. (2006) state that conservation of the natural *Echinacea* resources across North America has socio-political implications due to issues of private and public land tenure, especially on Aboriginal (i.e., Native American) land reserves. Governance of lands and natural resources tends to vary at the federal, state/provincial, or regional levels in both Canada and the United States. The majority (>90%) of natural *Echinacea* populations occur in the United States (Fig. 1.3), where there is a National Germplasm Conservation Program that addresses all *Echinacea* taxa among other resources and threatened species in collaboration with the Nature Conservancy, the State Departments of Natural Heritage/Conservation, and the US Department of Agriculture (USDA).

According to Brinker (2013), the popularity of *Echinacea* has resulted in regional overharvesting of wild *E. angustifolia*. Nonetheless, commercial cultivation of *E. purpurea* and conscientious wildcrafting can continue to provide a sustainable supply of these important botanical medicines. Cultivation of *Echinacea* species has increased rapidly because of the demand and its great value. Growth of the three major medicinal species, *E. angustifolia*, *E. pallida*, and *E. purpurea*, has been the most studied: among them *Echinacea purpurea* is easy to grow, as compared to the other two commercial species.

In an interesting paper by Foster (2017) in HerbalGram, the author expressively calls attention to the values of American medicinal trees, deeming them "Forest Gems". He states that rather than viewing trees as temples of life, humans – in the course of past civilizations – have tended to look at trees in terms of board feet for timber, cords for fuel, or even, as simple nuisances that prevent the soil from being pierced with a plow.

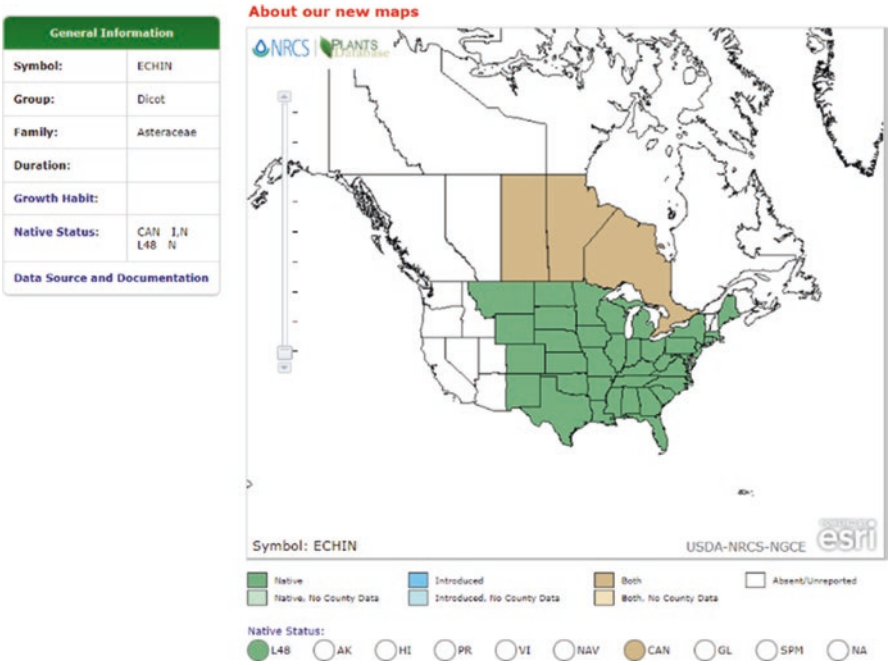

Fig. 1.3 North American distribution of Echinacea species. (USDA NRCS 2019)

1.6 Germplasm Conservation of MAPs in North America

Germplasm conservation in the United States is not new. Seed saving, replanting and management of wild landscapes is part of the pre-Columbian era traditional ecological knowledge of indigenous peoples of North America (Anderson 2006). Realizing the importance of genetic diversity, the USDA has been collecting and preserving germplasm since the late 1800s (Byrne et al. 2007). To accomplish this huge task a network of more than 25 active germplasm conservation sites (germplasm repositories, so called genebanks) was established under the coordination of the US Department of Agriculture (USDA) within the Agricultural Research Service's (ARS) National Plant Germplasm System (NPGS).

To date, the National Genetic Resources Program (NGRP) of USDA acquires, characterizes, conserves, documents, and distributes to scientists germplasm of all life forms important for food and agricultural production. It is the task of the Germplasm Resources Information Network (GRIN) to document these (animal, microbial, and plant) collections through informational pages, searchable databases, and links to USDA-ARS projects that curate the collections. GRIN is operated by the National Germplasm Resources Laboratory in Beltsville, MD.

The U.S. National Plant Germplasm System (NPGS) is collaborative effort to safeguard the genetic diversity of agriculturally important plants, including medicinal and aromatic species. NPGS's mission is to collect and conserve living plant

material of plants for food, fiber, animal feeds, industrial and medicinal purposes, and for landscape and ornamental uses. It also aims to help solve immediate agricultural production problems as well as safeguard plant genetic diversity for future needs. This task is accomplished by:

- acquiring crop germplasm,
- conserving crop germplasm,
- evaluating and characterizing crop germplasm,
- documenting crop germplasm,
- distributing crop germplasm.

As the primary focus of germplasm collections has traditionally been the long-term conservation of major crop species and their wild relatives with the ultimate goal to develop new varieties, medicinal plants have been under-represented. Consequently, a comprehensive facility dedicated to their conservation and research does not currently exist. Even the North Carolina Arboretum Germplasm Repository (TNCAGR) that due to the extraordinary botanical and chemical diversity of the southern Appalachians could be an ideal location for a medicinal plant germplasm repository, leads diverse activities leading to conserve, study and utilize native plants, explore alternative and new crops (including MAPs) for economic development purposes. From the viewpoint of MAPs the viewpoint of MAPs the National Germplasm Repository, in Corvallis (Oregon) with its blueberry, cranberry, hop, mint collections could be notable example for the important contribution genebanks (repositories) provide for the conservation of valuable natural genetic resources.

1.7 Cultivation of Medicinal and Aromatic Plants in North America

Earlier it was reported by Blumenthal (2004) that obtaining statistics on the actual amount of bulk herbal material grown or wild-harvested within the United States was a challenge. The U.S. Department of Agriculture's Foreign Agricultural Service maintains statistics on imported herbs and spices but there is no systematic process for measuring wild-harvested (a.k.a. wildcrafted) or commercially cultivated herbs used in the medicinal plant market. In the past few years, in its attempt to begin to quantify the wild-harvested raw materials used in the manufacture of various herbal products, the American Herbal Products Association (AHPA) has published five Industry Tonnage Surveys. The sixth survey is presently in preparation.

As regards the main cultivated and wild-crafted North American botanical crops, in the lack of relevant official data, Brinckmann's following compilation can provide some guidance (Brinckmann 2007) (Table 1.1):

In view of the increasingly strict quality requirements, American farmers have been implementing Good Collection and Agricultural Practices (GCAP). It was

Table 1.1 Main North American cultivated and wild-collected crops

Name of the plant species	Cultivated	Wild collected
Aloe vera:	Cultivated in Texas, and Tamaulipas, Mexico	
American ginseng root:	Cultivated in Ontario, Wisconsin;	Wild collected in 19 States
Black cohosh rhizome:		Wild collected in Kentucky, Tennessee, Georgia, Ohio, North Carolina, Michigan, South Carolina, Virginia,
Capsicum fruit:	Cultivated in New Mexico, Texas, Arizona, California,	
Cranberry fruit:	Cultivated in Wisconsin, Massachusetts, Canada, New Jersey, Oregon, Washington	
Echinacea herb & root:	Cultivated in Oregon, Washington, British Columbia;	In many Midwestern and Mid-southern States
Flax seed:	Cultivated mainly in Canada; also North Dakota, South Dakota, Montana, Minnesota	
Garlic bulb:	Cultivated in California	
Ginger rhizome:	Cultivated in Hawaii	
Hop strobile:	Cultivated in Oregon, Washington, Idaho	
Jojoba seed:	Cultivated in Sonoran Desert in Arizona, California and Mexico	
Lavender flower:	Cultivated in Oregon and Washington	
Peppermint leaf:	Cultivated in Oregon, Washington, Idaho	
Saw Palmetto fruit:		Wild collected in Florida
Spearmint leaf:	Cultivated in Oregon, Washington	

After: Brinckmann (2007)

most recently the United Natural Products Alliance (UNPA) that has endorsed AHPA's Good Agricultural and Collection Practices and Good Manufacturing Practices for Botanical Material and will encourage member companies to adopt AHPA's guidance.

In harmony with above efforts, providing regulations and guidance for sustainable agriculture, the USDA National Organic Program (NOP) was established by Congress, as early as 2001. (see: later this chapter).

Search for Higher Value Crops

American farmers looking for higher-value new crops: one of the options is to introduce and grow plants used by American practitioners of Traditional Chinese Medicine (TCM). The practice of acupuncture and Chinese herbal medicine is

authorized and regulated in 47 states and the District of Columbia. One of the heralds for this activity, Foster (Foster 2004), in a book co-authored with Professor Yue Chongxi,"Herbal Emissaries: Bringing Chinese Herbs to the West" documented the use of Chinese herbs in American gardens. It has been reported by Raterman (Raterman 2018) that the recently (in 2014) established Appalachian Herb Growers Consortium (AHGC) of small farmers, in southwestern Virginia, is engaged in using ecologically sustainable practices to grow Chinese medicinal herbs. Presently the consortium has some 50 small farmer members. Its mission is to bolster farmers' incomes and crop diversity; provide high-quality, effective herbs for practitioners of acupuncture and TCM; and grow and process herbs with respect for nature and the traditions of TCM.

Brinckman (Brinckmann 2015) also calls attention to the new trend to grow Chinese medicinal plants in North America. According to him, the areas mainly concerned are located in parts of rural eastern and southern United States where tobacco (*Nicotiana tabacum* L.; Solanaceae) leaf was once the main economic crop. Farmers in western North Carolina even claim that they share the same latitudes and elevations of the mountainous provinces in China so that are ideal for cultivation of certain Chinese medicinal plants.

Diversification of agricultural production has been an important issue for American farmers for decades. Presently, these activities are centered around university Extension and Outreach centers/programs. Probably the best known of these is the Center for New Crops & Plant Products, at Purdue University. Its web-site called NewCROP (https://www.hort.purdue.edu/newcrop/) provides windows to new and specialty crop profiles.

1.8 Medicinal plants in the North American Folk Medicine (Traditional Medicine)

Herbals/botanicals or herbal medicine (a plant or plant part or an extract or mixture of these) have been used to prevent, alleviate specific symptoms, or cure disease since ancient times of mankind.

According to Moerman (Moerman 2016), native American peoples developed a sophisticated "plant-based medical system" in the course of millennia before the European conquest of America. Despite the significant differences between the systems developed by the various native groups, there were also many broad similarities. Out of the approximately 28,000 species of plants in North America, native Americans used about 2500 medicinally (Moerman 1996, 1998); a comprehensive database of these plant uses is available in the database/book on **Native American Ethnobotany** (http://naeb.brit.org/).

The "Native American Ethnobotany" is perhaps best extensive on-line source of concise information about Native American uses of herbs, this site contains records of the historical uses of over 4000 species of plants by almost 300 North American

aboriginal groups. Presently, database is maintained by the University of Michigan, as an expression of lifelong commitment of Dan Moerman to that school. In a practical way, the current version is linked to the USDA PLANTS database so that taxonomic and range information can also be readily found for most of the listed species.

A quick analysis of the database reveals that the richest sources of medicines are the sunflower family 12 (Asteraceae), the rose family (Rosaceae), and the mint family (Lamiaceae). As a remarkable contrast, the 13 grass family (Poaceae) and the rush family (Juncaceae) contain practically no medicinal species. This outstanding volume and extraordinary selectivity demonstrate without any doubt the falseness of degrading claims that according to which Native American medicines were chosen at random, quasi they "just used everything and stumbled on something useful once in a while."

1.8.1 Traditional Medicines Congress (TM)

The TM Congress is a forum for meetings and communications between various U.S.- based organizations with a common interest in preserving access to traditional medicines and improving the free flow of information about the traditional uses of these medicines.

The TM Congress was founded in 2004, when a diverse group of professional organizations met to initiate a coalition/cooperation aimed at the exchange of ideas about the future of traditional medicines in the United States. The result was the convening of the Traditional Medicines Congress, presently sponsored by the following nine national organizations: Acupuncture and Oriental Medicine Alliance (AOMA), American Association of Naturopathic Physicians (AANP), American Association of Oriental Medicine (AAOM), American Herbalist Guild (AHG), American Herbal Products Association (AHPA), Council of Colleges of Acupuncture and Oriental Medicine (CCAOM), Medicinal Herb Consortium (MHC), National Ayurvedic Medical Association (NAMA), National Certification Commission for Acupuncture and Oriental Medicine, (NCCAOM).

According to its declaration (Congress n.d.) the "goal of the Traditional Medicines Congress is to benefit public health by ensuring access to traditional medicines in a manner that provides a reasonable expectation of public safety." The members (sponsors) of the TM Congress have elaborated and published a Draft Proposed Regulatory Model for Traditional Medicines, in 2006. It is believed „to provide a rational framework for truthfully representing the value of traditional medicines and for assuring widespread consumer access to herbal products". Key components of the regulatory frameworks are expected „to clearly define traditional medicines and ensure access to these while addressing safety, in the retail marketplace and in clinical settings".

Table 1.2 On-line herb book resources of traditional medicinal plants

Culpeper, Nicholas: *The English Physician*. **1652**	http://doc.med.yale.edu/historical-old/culpeper/culpeper.htm
United States Pharmacopoeial Convention: *The Pharmacopoeia of the United States of America*. **1820**	https://collections.nlm.nih.gov/ext/dw/2567001R/PDF/2567001R.pdf
Wood GB, Bache F: The Dispensatory of the United States of America, 1st edition. **1833**	https://collections.nlm.nih.gov/catalog/nlm:nlmuid-10430300R-bk
Felter, Harvey Wickes and John Uri Lloyd: *King's American Dispensatory*, 18th edition, 3rd revision. **1898**	http://www.henriettesherbal.com/eclectic/kings/index.html
Lloyd, John Uri: History of the Vegetable Drugs of the Pharmacopeia of the United States. **1911**	http://www.swsbm.com/ManualsOther/USP_Drug_History_Lloyd.pdf
Hedrick, UP: Sturtevant's Notes on Edible Plants. **1919**	http://www.swsbm.com/Ephemera/Sturtevants_Edible_Plants.pdf
Grieve, Maude: *A Modern Herbal,* 2 vol. **1931**	http://www.botanical.com/botanical/mgmh/comindx.html
Remington, Joseph P., Horatio C. Wood, et al.: *The Dispensatory of the United States of America*, 20th edition. **1918**	http://www.swsbm.com/Dispensatory/USD-1918-complete.pdf
Woodville, William: *Medical Botany*, 4 vol. 1790–1793	http://www.illustratedgarden.org/mobot/rarebooks/title.asp?relation=QK91C7431790V1

1.8.2 Historical Herb Books on Line

Due to space limitations, in our introductory chapter we cannot go into details about the description and historical use of native American herbs. The following table (Table 1.2) offers a basic list of comprehensive **on-line resources** that provide sufficient information for getting oriented about the multiplicity of traditions and uses North American traditional medicinal plants (Table 1.2).

1.8.3 Patented Medicines vs. Integrative Medicine

In the United States, patent medicines (proprietary medicines made and marketed under a patent and available without prescription) first became popular in the 1800s. Many of these were of plant origin and often had "secret formulations". They were often sold directly to consumers. (As there was no Federal regulation of these products until passage of the Pure Food and Drug Act of 1906 and subsequent United States Federal Food, Drug, and Cosmetic Act of 1938, consumers had no means to distinguish between false and valid claims.) Nearly simultaneously, the pharmaceutical industry was developing, and marketing its products directly to health professionals. Remarkably, similarly to the patent medicines, there were no regulations in place to assure health professionals or consumers of a given product's effectiveness and safety.

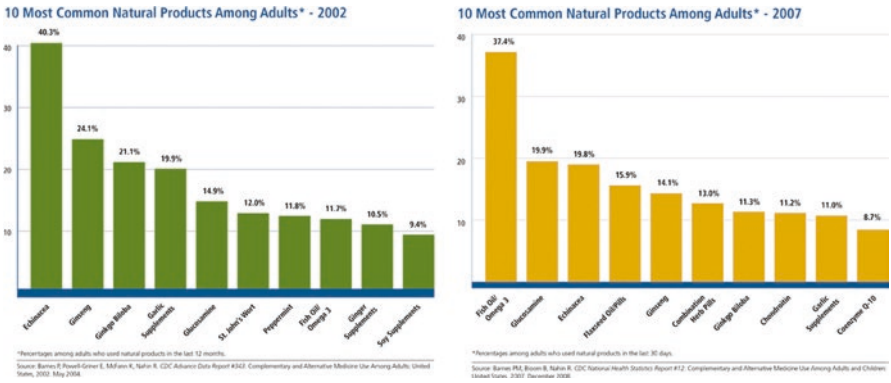

Fig. 1.4 10 most commonly used natural products among adults, in 2002 vs. 2007

By the early 1900s, the Federal Government enacted legislation to assure the characterization of effectiveness and safety of food and drugs. This step was largely driven by growing fraud within the respective industries (Barkan 1985).

In the subsequent decades, the interest of Americans population in self-care has been increasingly growing. In 2007, a spending of $33.9 billion out-of-pocket for CAM was reported which amounts to approximately 1.5% of total health care expenditures and more than 11% of total out-of-pocket health care expenditures. According to a survey by the National Center for Complementary and Integrative Health of National Institutes of Health (N.I.H.), in 2007, the most popular natural products were the following: fish oils/omega 3, glucosamine, echinacea, and flaxseed. In 2002, the most popular natural products were echinacea, ginseng, ginkgo, and garlic supplements (Barnes et al. 2008) (Fig. 1.4).

To-date, the National Center for Complementary and Integrative Health (NCCIH) is the Federal Government's lead agency for scientific research and on complementary and integrative health approaches: it is one of the 27 centers and institutes making up the National Institutes of Health (NIH) within the US Department of Health and Human Services.

NCCIH is striving to fulfil its mission „to define, through rigorous scientific investigation, the usefulness and safety of complementary and integrative health interventions and their roles in improving health and health care". As an "arbitrarily" chosen example from the multiplicity possible research topics, we refer to a recent study by Dettweiler et al. (Dettweiler et al. 2019) in which extracts from three plants (*Quercus alba*, *Liriodendon tulipifera* and *Aralia spinosa*) used as medicines during the American Civil War were tested and verified to show antimicrobial activity against multidrug-resistant bacteria associated with wound infections.

1.9 Botanical Drugs vs Herbal Dietary Supplements

In the U.S., botanical products, depending on the circumstances, may be regulated as botanical drugs (OTC, Rx, or Homoeopathic), non-drug cosmetics, herbal dietary supplements, or foods. American consumers' interest in health and self-care suggests that they are searching for alternatives to conventional foods for physical and mental well-being. There is a trend that with the increasing advent of food that is already worryingly synthetic and influenced by technology, a significant proportion of the US population is turning towards foods and medicines, including dietary supplements of plant origin. These they see as more natural (Mariott 2003). Dietary supplements of plant origin, roughly equate to botanical supplements or supplement ingredients.

As a result, to-date, there are more than 29,000 different dietary supplements available to consumers (Gibson and Taylor 2005), whereas the number of dietary supplement products made from plants is not exactly known.

The federal agency, Food and Drug Administration (FDA) is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, including medicinal and aromatic plants. The scope of FDA's regulatory authority is very broad. In view of MAPs, the topic of this chapter, the following responsibilities of FDA's should be highlighted: dietary supplements, food additives, prescription (Rx) and non-prescription (over-the-counter (OTC)) drugs), non-drug cosmetics, veterinary drugs, etc. However, this is not an exhaustive list.

Today, the FDA regulates $1 trillion worth of products a year. It ensures the safety and effectiveness of all drugs, biological products and animal drugs and feed, etc.

1.10 Market of Botanicals

To-date, modern herb trade is seen as part of a multi-billion dollar herb industry. In 2014, for the 11th consecutive year, American consumers spent more on herbal dietary supplements than they did in the previous year. Since 2011, estimated herbal supplement sales in all channels have increased by more than $1 billion; in 2014, US consumers spent roughly $400 million more on plant-based supplements than in 2013. These figures suggest a clear trend: Americans are continuing to rely on botanical products for various aspects of their wellbeing and other personal needs (Smith et al. 2015).

The sales data presented by Smith et al. (2015) reflect consumer preferences. In 2014, retail sales of combination herbal supplements and total supplement sales in natural and health food stores seemed to increase faster than other herbal supplement products and channels, respectively.

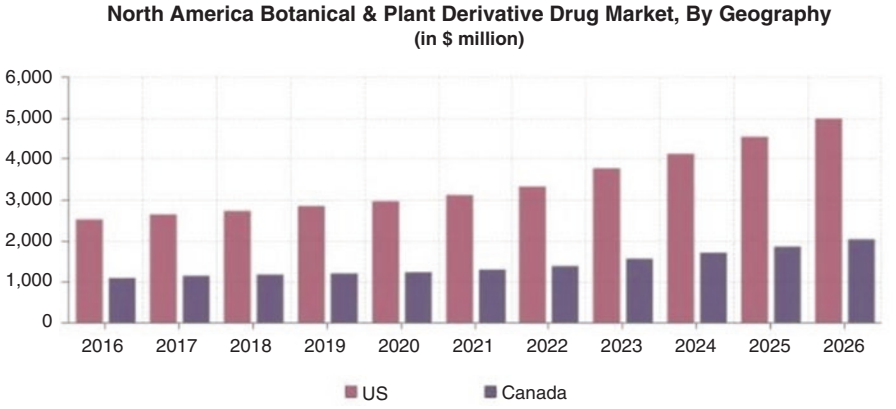

Fig. 1.5 North Amarican Botanical and Plant Derivative Drug Market. (Source: https://www.inkwoodresearch.com/reports/northamerica-botanical-plant-derivative-drug-market/)

According to estimates by Inkwood Research North America's Botanical and plant derivate drug market is deemed to see a farther steady growth (Fig. 1.5).

Total **retail sales of herbal dietary supplements** in the United States increased by an estimated 6.8% in 2014 marking the 11th consecutive year of growth (Smith et al. 2015). This increase is slightly less than 2013's 7.9% increase, which was the greatest percentage sales jump since the late 1990s.

Sales of herbal supplements have been increasing steadily since 2002–2003 when the market experienced a brief, two-year dip in total sales. American consumers spent roughly $6.4 billion on herbal supplements —over $1 billion more than was spent in 2011 and $400 million more than 2013 — according to aggregated market statistics provided by the *Nutrition Business Journal* (NBJ).

NOTE: A general comment regarding the content and structure of the following Sect. 1.11 on actors. You might consider organizing similar actors together. For example,

- **three compendia** (quality standards monographs) are discussed, the United States Pharmacopoeia (USP), the National Formulary (NF), and the American Herbal Pharmacopoeia (AHP). These could be listed one-after-the-other for coherence. There is another relevant official compendium not mentioned. The United States Pharmacopoeial Convention (USPC) actually produces three official compendia, the USP, the NF, and the Food Chemicals Codex (FCC): https://www.foodchemicalscodex.org/
- **two trade associations** are discussed, American Herbal Products Association (AHPA) and American Spice Trade Association (ASTA). These could be grouped together for coherence.
- **two regulatory agencies** are discussed, the U.S. Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA). There are other governmental agencies that impact the production, trade and use of botanicals in the

United States, e.g. the U.S. Fish and Wildlife Service (USFWS) as the CITES authority and the U.S. Environmental Protection Agency (EPA) regarding the establishment of tolerances for pesticides that can be used on botanical crops. The U.S. Drug Enforcement Administration (DEA) is also involved for drug companies that import controlled botanical drugs like coca leaf from Peru or opium exudate (or registered churches that import ayahuasca tea from Brazil). You might also consider discussing the government-funded National Center for Natural Products Research: https://pharmacy.olemiss.edu/ncnpr/

- **one educational organization** is discussed, the American Botanical Council (ABC). Another educational non-profit organization you might consider discussing is the American Herbalists Guild (AHG): https://www.americanherbalistsguild.com/

1.11 Actors of North American Medicinal and Aromatic Plants Industry

Herbal products are most versatile. They can be sold in various forms, e.g.: as conventional foods or food additives (e.g. flavoring or coloring agents), as dietary supplements, as cosmetic ingredients, or as botanical drugs, etc. Ultimately, they may also be used as self-collected plants that are not marketed products IARC (2016).

In the US and Canada, pharmaceutical drugs are subject to strict regulations, like in most countries. Their availability is similarly restricted. Remarkably, however, this may not be the case with materials used in the preparation of herbal medicines, although the therapeutic benefit of such herbal products may have been recognized in certain communities for centuries. Moreover, herbal products are available in several regulatory models, ranging from foods and dietary supplements to cosmetics and over-the-counter (non-prescription) and prescription drugs. As a result, product quality and composition may vary from country to country and even within countries, (e.g.: different products bear the same name) (International Agency for Research on Cancer 2016).

In view of the abovementioned, the following compilation has the aim of providing an insight into the multitude of actors that are influential in shaping, regulating the MAP scenery in North America.

1.11.1 Food and Drug Administration (FDA)

The Office of Food and Drug Administration of U.S. Department of Health and Human Services (FDA) regulates both finished dietary supplement products and dietary ingredients. For dietary supplements a different set of regulations are in

force than for those covering "conventional" foods and drug products. Under the Dietary Supplement Health and Education Act of 1994 (DSHEA):

No different than medicines, manufacturers and distributors of dietary supplements and dietary ingredients are prohibited from marketing products that are adulterated or misbranded. That means that these firms are responsible for evaluating the safety and labeling of their products before marketing to ensure that they meet all the requirements of DSHEA and FDA regulations.

FDA is responsible for taking action against any adulterated or misbranded dietary supplement, drug, or food product after it reaches the market.

The Dietary Supplement GMPs Final Rule and Interim Final Rule were effective August 24, 2007, introduced to help ensure the quality of dietary supplements so that consumers can be confident that the products they purchase contain what is on the label" (von Eschenbach 2007)" Farthermore, as a result of recent amendments to the Federal Food, Drug, and Cosmetic Act, by the end of that year, industry became required to report all serious dietary supplement related adverse events to FDA."

Remarkably, the final rule included flexible requirements that later on, can evolve with improvements in scientific methods used for verifying identity, purity strength, and composition of dietary supplements.

As a companion document, in an interim final rule, outlines for a petition process has also been issued for manufacturers to request an exemption to the cGMP requirement for 100% identity testing of specific dietary ingredients used in the processing of dietary supplements.

1.11.2 Pharmacopoeia of the United States of America (USP)

The United States Pharmacopoeial Convention (USPC) is responsible for several official compendia with monographs that are incorporated into regulations. These include the United States Pharmacopoeia (USP), the National Formulary (NF), and the Food Chemicals Codex (FCC). The Federal Food, Drug, and Cosmetic Act (FD&C Act) defines the term "official compendium" as the official USP, the official NF, and the official Homeopathic Pharmacopeia of the United States (HPUS). The USP-NF produces monographs for botanical ingredients that are used as active ingredients of botanical drugs (Rx and OTC), components of herbal dietary supplement products, and as excipients (food additives and pharmaceutical aids).

According to http://www.usp.org/about USP has the mission to improve global health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods. USP approaches this vision with a sense of urgency and purpose, strengthened by its cadre of dedicated volunteers, members, and staff, and by working collaboratively with key stakeholders across the globe.