

Regulatory Framework Of Herbal Medicine In Mexico

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Abstract

Recently there has been a shift in universal trend from synthetic to herbal medicine, which we can say "Return to Nature". Medicinal plants have been known for millennia and are highly esteemed all over the world as a rich source of therapeutic agents. Botanical medicine represents an important share of the pharmaceutical market. Natural products compounds discovered from medicinal plants (and their analogues thereof) have provided numerous clinically useful drugs in the treatment of chronic and or acute disease and still remain as an essential component in the search for new medicines. So, these traditionally used plants can be explored effectively in order to find New Chemical Entity for the treatment of chronic and acute disease. The herbal industry shares about US \$100 billion with good growth potential. Hence this field is having greater future perspectives. Review was performed systematically by review of literature published in journals and websites of different regulatory agencies, then after study of all the literatures which will summaries details related to registration of herbal product in Mexico. It covers legal aspects, procedural details, GMP and labeling requirements. It is very common trend globally to register herbal medicines and Mexico is one the country in that list. So the present work might provide a path for pharmaceutical companies who wise to sell their product in Mexico. This paper gives details about registration of herbal medicines in Mexico.

Keywords:- Herbal medicines, GMP, Scientific names, Regulatory Agency, Mexico

1.0 Introduction

Conventional medicines are those which contain traditional knowledge that developed over generations in various cultures. The oldest record of herbal medicine is found in Indian, Chinese, Greek, Roman, Syrian and Egyptian literature science about 5000 years.¹ As per WHO about 80% of world population is using products based on medicinal herbs and Plants and market share of conventional medicine is increasing exponentially.² As per the World Bank report there is about 15% growth in the trade of medicinal plants and raw materials. As number of patients seeking alternate and herbal therapy is growing globally However, recent findings indicate that all herbal medicines may not be safe as severe consequences are reported for some herbal drugs.³ Most herbal products in the market today have not been subjected to drug approval process to demonstrate their safety and effectiveness. So regulatory agencies are also working continuously to set perfect regulatory framework for manufacturing and marketing of herbal products. But transformation of traditional knowledge in to modern regulatory frameworks is a big challenge. The Mexico guidelines on for cultivation and collection of medicinal plants advise local

regulatory body for different aspects of herbal medicine for collection methods, site selection, climate and soil considerations and the correct identification of seeds and plants. These guidelines also contain guidance for labeling and legal component for quality standards.⁴ In this paper we are trying to collect information's related to the regulatory approval of herbal drug in Mexico which will be helpful to understand the approval procedure and regulation for herbal medicine.^{5,6}

2.0 How to market Herbal Medicine in Mexico

2.1 Herbal remedy:

Preparation or parts of a medicinal plant, alone or combined, and derivatives presented in a pharmaceutical form whose popular or traditional knowledge has attributed properties for the relief of symptoms of a disease. Such remedies should not contain psychotropic or narcotic drugs, hormonal products or substances in concentrations representing any risk for health. Plants used as raw material should be sanitized according to the current norms or specifications. According to Art. 92 of the Regulation of Healthcare Products, to market an herbal remedy, COFEPRIS will issue an authorization corresponding to and alphanumeric key (*clave alfanumérica*) after presentation of the appropriate documentation.⁷

2.2 Herbal medicinal products:

Products manufactured from vegetable material or derivatives whose main ingredients are portions of plants or standardized extracts, dyes and juices or resins, fatty or essential oils, in a pharmaceutical form whose therapeutic effect and safety has been confirmed in either national or international scientific literature (General Law of Health Art. 224). Herbal medicinal products may include in their formulation excipients and additives (Art. 66 Fraction III of the Regulation of Healthcare Products).⁸

This definition does not include synthetic psychotropic or narcotic substances, mixtures with allopathic drugs, procaine, ephedrine, yohimbine, chaparral, germanium, animal or human hormones and other substances with hormonal activity as well as other products representing risk for health (Regulation of Healthcare Products Art. 66 to 68).⁹ Isolated and chemically defined active ingredients and products for injection are not considered as herbal products. Herbal medicinal products are subject to sanitary registration before commercialization. Plants prohibited for use in herbal remedies and teas are listed below (Source: *Diario Oficial de la Federación*, 15-Dec-1999)¹⁰

2.3 Scientific name/ Common name¹⁰

- *Acacia gregii* Acacia
- *Aconitum napellus* L. Aconite
- *Acorus calamus* Calamus
- *Aesculus hippocastanum* L. Chestnut of indias
- *Apocynum cannabinum* Hemp plant of Canada, Apocino
- *Arnica Montana* L. Arnica
- *Artemisia absinthium* L. Common absinth
- *Artemisia maritime* L. *Artemisia cina* Marine absinth
- *Artemisia vulgaris* L. Absinth

- *Atropa belladonna* L. Belladonna
- *Berberis vulgaris* L. Agracejo
- *Bryonia dioica* L. White bryony
- *Cinnamomum camphora* Seib. Camphor
- *Colchicum autumnale* L. Colchicum
- *Conium maculatum* L. Cicuta
- *Convallaria majalis* L. Convalaria, Lily
- *Croton tiglium* L. Croton
- *Cystisus scoparius* L. Black broom
- *Chelidonium majus* L. Celandine
- *Chenopodium ambrosioides* Epazote, Pazote
- *Chrysanthemu spartheniun* Matricaria
- *Daphne laureda* L. Laurel
- *Daphne mezereum* L. Mezereon
- *Daphne* spp. *Daphne gnidium* L. Spurge flax
- *Datura stramonium* L. Stramonium, Fig tree, Toloache
- *Digitalis purpurea* L. Digitalis
- *Dipteryx odorata* Willd Butter bean, Sarrapia, Cumerona
- *Euonymus atropurpureus* Evónimo
- *Euonymus Europeans* L. Evónimoeuropeo
- *Eupatorium rugosum*
- *Euphorbia characias* L. Caracias
- *Euphorbia* spp *Euphorbia lathyris* L. Tartago
- *Exogonium purge Wenderoth* Jalapa
- *Gelsemium sempervirens* L. Gelsemium, honeysuckle
- *Coryanthe yohimbe* Yohimbina
- *Hedeom apulegioides* L. Pers. American poleo, Hedeoma
- *Heliotropium european* L Heliotrope, Verrucaria
- *Hyoscyamus niger* L. Black henbane
- *Hypericum perforatum* L. Hipericum
- *Illicium anisatum* Star anise
- *Ipomoea purpurea* L. Common morning glory
- *Juniperus sabina* L. Sabina
- *Lantana camara* L. Five little black, catnail, Alantana
- *Larrea tridentate* Creosote bush, Gobernadora
- *Lobelia inflata* L. Lobelia
- *Mahonia aquifolium* (Pursh) Nutt.
- *Mandragora officinarum* L., *Mandragora autumnalis* I. Mandragora
- *Mentha pulegium* L. Poleo
- *Narcissus pseudo-Narcissus* L. *Narcissus poeticus* L. Narcissus
- *Pausinystalia yohimbe* Yohimbina
- *Phorandendron flavescens* (Pursh) Nutt. Mistletoe

- *Phoradendron juniperinum*
- *Physostigma venenosum* Balf. Haba de calabar, Nuez de esere
- *Phytolacca Americana* L. Carmine herb
- *Podophyllum peltatum*L. Podophyllum
- *Rauwolfia* spp. Rauwolfia
- *Ricinus communis*L. Ricinus
- *Sanguinaria canadensis* L. Canadian sanguinaria
- *Sarothamnus scoparius* WIMMER Retama de escobas
- *Sassafras albidum* (Nutt) Nees.Sasafrás
- *Senecio aureus* L. Senecio dorado
- *Senecio jacobaea* L. Hierba de Santiago
- *Solanum dulcamara* L. Dulcamara
- *Strophantus gratus* (Hook) Baill, Kombé
- *Strophantus kombe* Oliver Estrofanto
- *Strychnos nux-vomica* L. Vomica nut
- *Symphytum asperum* Lepech
- *Symphytum officinale* Consuelda
- *Symphytum Xuplandicum* Nym
- *Tanacetum vulgare* L. Tanaceto
- *Thuja occidentalis*L. Arborvitae, tuya
- *Tussilago farfara* L. Farfara
- *Veratum album* L. White hellebore
- *Vinca minor* L. Vinca
- *Viscum album* L.Mistletoe
- *Withania somnifera* (*Strychnos hypnotica*)Orovale.
- *Arctostaphylos uva-ursi* L. Gayuba
- *Caulophyllum thalictroides* Blueberry root
- *Cimicifuga racemosa* Cimicifuga, culebranegra roof
- *Hydrastis canadensis* L. Canadian roof
- *Liupiadulcis* Sweet herb
- *Montanoa tormentosa* Zoaplatle
- *Petroselinum crispum* Parsley
- *Ruta graveolens* Ruta
- *Salvia officinalis* L.Salvia.

3.0 Legal basis and regulatory framework¹¹

a) Herbal remedies:

General Law of Health (*Ley General de Salud*), Art. 223, 370, 371 and 378. Regulation of Healthcare Products, Arts. 88 to 98.

b) Herbal medicinal products:¹²

General Law of Health (*Ley General de Salud*), Arts. 221, 222, 224 to 227, 368, 371, 376, 376 bis Fraction I and 378. Regulation for Healthcare Products, Arts. 165 to 175, 177 and 178.

The Law establishes that all products with an indication for the prevention or treatment of illnesses have to receive an authorization. Herbal medicines and remedies can be sold without prescription as over-the-counter (OTC) products. The Pharmacopoeia Commission is responsible for reviewing monographs. No review is done prior to registration.

A new agreement was proposed in April 2012 "*Acuerdo por el que se determinan las plantas prohibidas opermitidas para tés, infusiones, aceites vegetales comestibles y suplementos alimenticios*" still under review as the text doesn't mention medical use. The health authorities are reviewing the agreement to correct it since they are taking away 197 plants as dangerous ones - including "Aloe Vera" which represents a risk for the local economy.¹³

3.1 Listing/Catalogue¹⁴

The lists of well-established use products and allowed plants can be found at the Herbal Mexican Pharmacopoeia (*Farmacopea de Herbolarios*).

The list of allowed plants is:

- Wormwood herb
- Alholva semilla (*Trigonella foenum-graecum*)
- Aloe vera
- Japanese aralia root (*Fatsia japonica, Aralia japonica*)
- Angelica root (*Angelica archangelica*)
- Anise plant *Pimpinella anisum*
- Arnica flowers
- Peruvian balm
- Henbane leaf (*Hyoscyamus niger*)
- Belladonna leaf (*Atropa belladonna, L*)
- Belladonna root
- Boldo hoja
- Borraja flor (*Borago officinalis, L*)
- Cinnamon
- Cardamom fruit
- Cáscara sagrada corteza
- *Centaurium erithraea* herb
- Colombo root
- Damiana leaves
- Quickset / hawthorn fruit
- Eucalyptus leaf
- Gayuba leaf
- Gentian root

- Gingko biloba leaves
- Ginseng root
- Hamamelis leaf
- Harpagofito root
- Mint leaves
- Fennel bitter fruit
- Ipecacuanha root
- Jamaica flower
- Juniper fruit
- *Humulus lupulus* hop
- *Camomile* flower
- Marmalade orange/biter orange shell
- Plantago seeds
- Poligala root
- Quina cortex
- Rhubarb root
- Sant Mary herb
- *Cassia Angustifolia* Senna leaves.

4.0 Registration of herbal medicinal products¹⁵

The format and content of an application is different from the Standard Format for a medicinal product (a simplified dossier is required).

a. Herbal remedies: use the Standard form Form: Application for Authorizations, Certifications and Inspections with the “*Homoclave: Solicitudde Clave Alfanuméricade Remedios Herbolarios*”.

4.1 COFEPRIS-04-009-A

Request of alphanumeric key for Herbal Remedies. Category A. National manufacture. The application should include the following data and supporting documents: Application form; Original and two copies of the proof of payment; Certificate of analysis of the finished product showing the organoleptic, physical and microbiologic properties of the plant, as well as the absence of toxic residues; Description of the manufacturing process, according to Good Manufacturing Practices; Authentication certificate for each component or document containing information on the components identity;

1. Scientific and common denomination of used plant(s)
2. Indications and time of use
3. Labeling proposed text
4. Quail quantitative formula of all components and additives, (signed by the sanitary responsible).

If imported (*Homoclave COFEPRIS-04-009-B*):

1. Certificate of analysis, issued by the manufacturer, with letterhead, signed by the responsible chemist of the national/foreign company;
2. Good Manufacturing Practices certificate (original or certified copy);
3. Representation letter (except for products manufactured by the subsidiary of the

Marketing Authorization Holder in Mexico).

b. Herbal medicinal product: The form to be used is the standard one named Form: Application for Authorizations, Certifications and Inspections. The codes to be used are the following ones:

C. Marketing Authorization for Herbal medicinal products.

Category A.- National manufacture.

The Instructions provide the main information to be submitted in the Registration dossier and the content of application:

1. Technical and scientific information demonstrating the identity and purity of compounds (+ Certificate of analysis):
 - Description of the primary and secondary packaging
 - Identification method for the active ingredient(s)
2. Technical and scientific information demonstrating the stability of the finished product (+ certificate of analysis). Certificate of taxonomic identification for each part of the plant, or document proving the components identity.
3. Therapeutic indications;
4. Draft of the labels;
5. Instructions for use (if applicable);
6. Description of the manufacturing process of the Herbal medicine to be registered;
7. Prescribing information.

The application should be sent to the main office located at: Calle Oklahoma No. 14 Colonia Nápoles - Delegación Benito Juárez Código Postal: 38100 Ciudad de México. The review process starts with stamping the application which is given to one Pharmacist or Chemist for review. After this technical review the officer issues a written opinion and turns it to the Physician for clinical/medical review. The second reviewer provides the final opinion to be delivered. If the information is considered to fulfill the MOH requirements, the marketing authorization is granted and the official document is delivered.

5.0 GMP Certificates

According to Art. 222 of the General Law of Health, a GMP certificate should be submitted to obtain a marketing authorization. The GMP certificate is the document proving the compliance of the manufacturer with such requirements. For herbal medicinal products, the documents issued by the Health Authorities of the country of origin, that have an agreement with the Mexican Office of Health and comply with the proving that the manufacture is in compliance with the Good Manufacturing practices, will be accepted, if they are issued in countries where herbal medicinal products are considered as dietary supplements (explaining that such Authorities would not issue a GMP certificate as for medicinal products), in accordance to the Guidelines on the requirements to be fulfilled to Obtain a Good Manufacturing Practice Certificate when Applying for Marketing Authorization, Renewal or Variation For medicines manufactured abroad, the following considerations have to be taken in account:

1. That interested company to make a request to COFEPRIS, presents the Certificate of Good Manufacturing Practices or Equivalent Document: These documents are the Certificates of Good Manufacturing Practices issued by competent local or federal authorities of the origin country that guarantee the medicament or API was produced under Good Manufacturing Practices.
2. For those products that are considered nutritional supplements in the origin country the document authorized to be presented is the Equivalent Document issued by the competent regulatory authority.
3. The Certificate will have duly legalized by a postilled.
4. The certificates or declarations emitted by the medicaments or API manufacturers, in which it is pronounced to produce them under GMP shall not be held as valid.¹⁶

For more information in the case of the present active ingredients in the formulation of herb medicaments, vitamin medicines that in its composition contain solely vitamins or minerals like mono or poli-drugs and homeopathic medicaments please refer to Good Manufacturing Practice and Inspections and Guidelines on the requirements to be Fulfilled to Obtain a Good Manufacturing Practice Certificate when Applying for Marketing Authorization, Renewal or Variation Certificates issued by the manufacturers, indicating that the manufacture is performed in compliance with the GMPs, will not be accepted. GMP certificates should be legalized, according to the Art. 153 of the Regulation of Healthcare Products, and translated to Spanish by a certified translator if issued in a different language. Official Mexican Norm NOM-073-SSA1-2015 establishes the requirements when carrying Stability studies with these products.

6.0 Labeling

a. Herbal remedies

The primary package should include the statement “*RemedioHerbolario*” (Herbal remedy), brand name, scientific name, popular name, pharmaceutical form and content (Declaration of formula, per volume or mass and equivalence, route of administration, use, information for storage and expiry date, authorization number with alpha numeric code: "RH". Also include batch number, manufacturer and distributor information: name and address.

Legends: Recommended use: ... followed by the expression:

“*La recomendación de uso de este producto se basa en la medicina tradicional de: _____, no en estudios científicos.*” (This recommendation is based on traditional medicine of: _____, not based on scientific studies”

How to use the product with precise directions for a correct preparation and dispensation of the Herbal remedy.

Warnings for pregnancy and breast feeding, contraindications, precautions and warnings for pediatric use, adverse reactions, interactions, overdose.

b. Herbal medicinal products

The same requirements as established for pharmaceutical and biotechnological products apply to Herbal medicinal products (see section [Product Information](#))

7.0 Post registration activities

7.1 Advertising

Advertising is allowed, as over the counter medications, only approved claims. A special statement: “Ask your doctor”.

8.0 Conclusion:

Because herbal drugs are inexpensive and also have better cultural acceptability, better compatibility with the human body and believe to have minimal side effects there many consequences of side effect have been seen in many cases. As herbal market is having a great future economic prospect. Systematic research and regulatory frame work is needed for further development.

This article provides all the basic information about the registration of Herbal medicine in Mexico. It also covers some additional major prospective like legal, labelling etc. It also summaries many example and resources with legal references however there are many other regulations which can play important role in this subject. These regulations will be developed in future as well with further additional minor details so herbal medicine can reach out to Mexican population.

References

1. Singh, A., Saharan, V. A., Kharb, V. & Bhandari, A. Current Status of Regulations for Herbal Medicines in Europe , United States and India. **2**, 406–422 (2011).
2. Asl Roosta, R., Moghaddasi, R. & Hosseini, S. S. Export target markets of medicinal and aromatic plants. *J. Appl. Res. Med. Aromat. Plants* **7**, 84–88 (2017).
3. Gunjan, M. & Ahmad, A. *MARKETING TRENDS & FUTURE PROSPECTS OF HERBAL MEDICINE IN THE TREATMENT OF VARIOUS DISEASE Analytical method development and dissolution profile of duloxetine and methylcobalamin by Vierodt's method View project Antimicrobial activity of Tinospora crispa root extracts View project*. <https://www.researchgate.net/publication/312172083> (2015).
4. Prasad Giri, R., Gangawane, A. K. & Ghorai Giri, S. REGULATION ON HERBAL PRODUCT USED AS MEDICINE AROUND THE WORLD: A REVIEW. *Int. Res. J. Eng. Technol.* **217**, (2008).
5. Rodriguez-Fragoso, L., Reyes-Esparza, J., Burchiel, S. W., Herrera-Ruiz, D. & Torres, E. Risks and benefits of commonly used herbal medicines in Mexico. *Toxicol. Appl. Pharmacol.* **227**, 125–135 (2008).
6. Winslow, L. C. & Kroll, D. J. Herbs as medicines. *Archives of Internal Medicine* vol. 158 2192–2199 (1998).
7. <http://dof.gob.mx/index.php?year=1999&month=12&day=15>
8. <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745>
9. https://ec.europa.eu/health/sites/health/files/endocrine_disruptors/docs/cosmetic_1223_2009_regulation_en.pdf
10. http://www.sice.oas.org/TPD/MEX_URY/MEX_URY_e.asp
11. <https://www.mindbank.info/item/2961>
12. <http://www.herbolariamexicana.com.mx/cofepris%20prohibe/Lista%20de%20Plantas%20Prohibidas%20de%20la%20Cofepris.pdf>
13. <http://staging.herbogram.org/resources/herbogram/issues/123/table-of-contents/hg123-herbprofile-hintonia/>

14. https://www.claa.org.mx/cir_pdf/2010/AnexoCirCLAA14810_SALUD.pdf
15. <https://www.gob.mx/cofepris/acciones-y-programas/otras-autorizaciones-tramites>
16. https://www.gob.mx/cms/uploads/attachment/file/348649/Instructivo_Autorizaciones.pdf