

Mexican Plants with Teratogenic Effects

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In Mexico, the use of medicinal plants is the first alternative to treat the diseases of the most economically vulnerable population. Some species with teratogenic effects and the main alterations that were found in the nervous system and axial skeleton, induced by compounds such as alkaloids, terpenes, and flavonoids.

[traditional medicine](#)[Mexican plants](#)[alkaloids](#)[Teratogenesis](#)[Sacred plants](#)

1. From Plants to Drugs

According to the significance that Greece, the cradle of philosophical thought and Western civilization, has held in the sciences and arts, it should not come as a surprise to us that the Greeks were the fathers of Medicine, Botany, and Pharmacology (Hippocrates, Theophrastus, and Pedanius Dioscorides, respectively), who laid the foundations of the therapeutic value of medicinal plants through detailed compilations of the knowledge of medicinal plants during their respective times and in their respective regions ^{[1][2][3]}, as well as that herbal medicine is denominated phytotherapy, a compound word formed by the Latin prefix *phyto* “plant”, and the Latin word *therapia*, “to treat medically”, in the study of the use of extracts of natural origin as medicines ^[4].

With the fall of the Western Roman Empire (476 AD), there began a period of time that stretched from the V to the XV century, called the “Middle Ages” or the “Dark Ages”, which involved a notable lag in the development of the sciences ^[5], despite that knowledge on the use of medicinal plants (and many others) survived during being confined for several centuries inside the walls of monasteries in countries such as England, Ireland, France, and Germany ^[6], among others. The Arab people were responsible for the preservation of a great part of Greco–Roman knowledge (along with that of the Chinese and the Indians, mainly in terms of plants), and later with the establishment of the first private pharmacies in Baghdad, Irak, at the end of the 8th century ^{[7][8]}. Later, the Persian pharmacist and poet Avicena (980–1037 AD) contributed to the dissemination of the knowledge of therapeutic plants with his work “*Canon Medicinae*”, considered the latest translation of all Greco–Roman Medicine ^[9] and the starting point for the development of medicinal-plant texts throughout Europe, such as “*The Corpus of Simples*” by Ibn al-Baitar, or the Florentine “*Nuovo Receptario Composito*”, which, alongside other manuscripts in England (1518), laid out the concept of “pure compounds” and promoted their development; a century later, these manuscripts would comprise the basis of the emergence of the first pharmacopoeia (First London Pharmacopoeia) ^[10]. Deriving from this idea, the first natural product to be marketed as isolated and pure was morphine, by Merck in 1826; while the first semi-synthetic medicine based on a natural product was aspirin by Bayer in 1899 ^[11].

The health needs of the increasing population have intensified the interest in developing more effective chemically synthesized compounds. In this context, since 1910, there was the “magic bullet” (Salvarsan or compound 606) by the German bacteriologist Paul Ehrlich [12], continuing all the way to modern times with the development of drugs used for chronic obstructive pulmonary disease, such as umeclidinium bromide [13]. Despite the good results obtained with chemical synthesis, the therapeutic potential of medicinal plants was not lost from sight. From plants such as meadowsweet (*Spiraea ulmaria*), poppy (*Papaver somniferum*), foxglove (*Digitalis purpurea*), and barbasco (*Lonchocarpus utilis*), drugs as remarkable as acetylsalicylic acid [14], morphine [15], digoxin [16], and diosgenin [17], respectively, have been obtained. Currently, this approach has become diversified thanks to the boom in novel processes for the extraction and identification of organic compounds, but mainly due to the increasing use of traditional medicine, which has been the starting point for information obtained throughout scientific research for the development of molecules that, under different conditions, would have been difficult or virtually impossible to conceive. In this regard, nature arises and is constituted, with chemical synthesis [18] and with biotechnology [19], one of the three main ways to obtain biologically active molecules today [20]. This said fact can be observed as reflected in the growing number of studies during the last decades that have provided valuable information to this scientific field, confirming the molecules present in the structures of numerous plants that possess a biological effect against diseases. However, in addition to the development of the knowledge of plant curative properties, the misconception of the safety of natural products has become a health problem that can be confirmed in several epidemiological and experimental assays.

2. Mexican Plants

Worldwide, Mexico has one of the richest diversities of plants composed of native and introduced species from various parts of the planet [21] that, together with their cultural wealth, constitute Mexican Traditional Medicine. In general terms, the concept of traditional medicine refers to a conventional denomination adopted by researchers to refer to empirical medical systems that are organized and based on various cultures of the world [22]. Thus, traditional medicine is made up of three main types according to the source of the remedy: that obtained from animal products; that of processed minerals, and Botany [23]. With regard to the latter, it is difficult to accurately determine the number of families, genera, or species of existing Mexican plants. Some reports estimate that Mexico has approximately 22,351 species of vascular plants (native and introduced) and calculate that at least 6500 species must be added to this calculation [24][25]. Of this total number (≈29,000 total vascular plants), it is suggested that between 3000 and 5000 plants are currently utilized with medicinal purposes in the country [26].

The Teratogenic Effects of Mexican Plants

During pregnancy, the organogenesis phase is the most critical period for generating birth defects, because it is at this time that the differentiation and specialization of tissues, structures, organs, and systems in the *conceptus* begin, with the grouping of cells in early patterns directed by gene expression toward specific sites in an organ [27]. Thus, during this period, it is most likely (but not exclusively so) that there occurs a multifactorial process known as teratogenesis. The latter, as a result of multiple interactions between environmental (physical, chemical, biological, and maternal diseases, clinical states, etc.) and endogenous (genetic background of the

mother and the embryo/fetus) factors, can produce a wide range of congenital deformities in the developing fetus or in the newborn [28]. Although the mechanisms by which this process occurs are varied, the main ones include oxidative stress, folate antagonism, vascular disruption, neural crest cell disruption, endocrine disruption, and specific receptor- or enzyme-mediated actions, among others [29]. Therefore, the severity and type of alterations will depend, among other things, on the time of the interaction of the teratogenic agent with the embryo/fetus, as well as on the mechanism(s) involved in the disruptive process.

The wide diversity of plants in Mexico allows some of these to be used by humans to alleviate their diseases or as food [30][31], even for livestock. In Mexico, as in other developing countries, the use of medicinal plants remains the first health care available in many rural areas to alleviate the diseases of the most economically vulnerable population, without social security [32][33], as a substantially less expensive and affordable alternative to conventional therapies. Unfortunately, in this practice, quality is generally unproven and is solely based on the population's beliefs. In contrast, insufficient attention is paid to their possible toxicity (unlike what happens with drugs), with the belief espoused for generations, e.g., “the natural remedy” is totally safe, without taking into consideration that plants could contain toxic compounds. Thus, although plants are undeniably an important source of health for vulnerable persons, it is important to make it known to the general population that “natural is not always safe”.

The data provided by several investigations demonstrate that an important number of herbs and herbal products have been implicated in poisoning [34], health problems [35], and alterations in embryonic/fetal development in humans [36] and animals [37]. This latter toxic effect of plants comprises an important problem worldwide, not only for public health, where birth defects are one of the main preventable causes of morbidity, mortality, and childhood disability [38], but also in the economic sector, since in different parts of the world, the consumption of teratogenic plants by pregnant females produces a wide variety of congenital anomalies in livestock, generating, in this manner, considerable losses of capital for companies and local ranchers [39].

3. Sacred Plants from Mexico

Additionally, it is important to consider that there are some species of Mexican plants that contain considerable amounts of the most common teratogenic compounds in nature, that is, alkaloids, but their teratogenic effect, to our knowledge, has not been investigated. Such is the case of *Borago officinalis* [40], the genus *Senecio* [41], and, of course, an important group of Mexican plants termed “sacred” (Table 1). In ancient Mexico (before the Spanish Conquest), plants with toxic properties were usually considered sacred, because their consumption induces mystical outbursts, fear, and alteration of the human mind in order to experience an elevation in consciousness; for this reason, they were bestowed with the personality of deities based on their effects [42]. In this manner, even today, the act of consuming *peyote* (*Lophophora williamsii*, America's most famous sacred hallucinogen) is called by an indigenous group, the *Huicholes*, as receiving “*hikuri*,” which means receiving the “heart of the Deer God,” who in turn is known as *Tatewari* and represents the grandfather god (God of Fire). This deity, the original shaman, collects *peyote* every year and guides his followers on a mystical pilgrimage to a sacred place where their ancestors rest: *Wirikuta* [43].

The Mexican sacred plants mentioned in **Table 1** possess an important role in rituals and in their medicinal use due to the presence of psychoactive alkaloids, such as psilocybin, mescaline, and ergotamine, among others [44]. However, an important case that needed to be specified here is that of *Salvia devious* or *hierba de la virgen*, which contains a powerful hallucinogenic substance called “salvinorin A,” with a structure similar to that of alkaloids. Nonetheless, it does not contain any nitrogen atom, and, thus, it is not considered as one of these, but rather the first documented diterpene nonalkaloid hallucinogen [45][46][47].

The use of plants with ornamental, nutritional, aromatic, medicinal, and religious purposes is widely extended in Mexico [48]. In this respect, sacred plants with biological effects comprise an important element in indigenous medical and religious practices [49]. According to the lack of studies found in this entry to evaluate the risks of these sacred plants for embryonic and fetal development, which are commonly used in Mexico, it is necessary to emphasize the danger of their use in the indigenous medical and religious systems. Although it is true that Mexico, in subscribing to international treaties, is obliged to prohibit any substance decreed by the World Health Organization (WHO), there is no law in Mexico that punishes the use of these substances. In other words, Mexican legislation sanctions the possession, but not the consumption, of illegal substances, including sacred plants. Therefore, the consumption of hallucinogenic plants such as *peyote* is legal with only certain restrictions (trafficking) that do not apply to indigenous groups because “ot is an issue of rights regarding the culture and native communities of our country” [50].

Table 1. List of Mexican sacred plants without studies of teratogenicity.

Scientific Name	Common Name	Compound	Type	Cite
<i>Ariocarpus retusus</i>	Peyote cimarron	Alkaloids	Cactaceae	[51]
<i>Argemone mexicana</i>	Chicalote	Alkaloids	Plat	[52]
<i>Conocybe</i>	Teonanácatl	Alkaloids	Mushroom	[53]
<i>Coryphantha compacta</i>	Biznaga Partida Compacta	Alkaloids	Cactaceae	[54]
<i>Datura ceratocaula Ortega</i>	Torna loco	Alkaloids	Plant	[55]
<i>Datura inoxia Mill</i>	Toloache	Alkaloids	Plant	[56]
<i>Echinocereus triglochidiatus</i>	Alicoche Copa de Vino	Alkaloids	Cactaceae	[57]
<i>Epithelantha micromeris</i>	Ikuli mulato	Alkaloids	Cactaceae	[58]
<i>Erythrina americana Mill</i>	Zumpantle	Alkaloids	Plant	[59]
<i>Heimia salicifolia</i>	Sinicuichi	Alkaloids	Plant	[60]
<i>Ipomoea violacea</i>	Quiebra platos	Alkaloids	Plant	[61]
<i>Lophophora williamsii</i>	Peyote	Alkaloids	Cactaceae	[62]

Scientific Name	Common Name	Compound	Type	Cite
<i>Lycoperdon mixtecorum</i>	Hongo de primera clase	Alkaloids	Mushroom	[63]
<i>Mammillaria senilis</i>	Biznaga cabeza de viejitos	Alkaloids	Cactaceae	[54]
<i>Pachycereus pecten-aboriginum</i>	Cardón Barbón	Alkaloids	Cactaceae	[64]
<i>Panaeolus sphinctrinus</i>	Toshka	Alkaloids	Mushroom	[65]
<i>Psilocybe caerulescens</i>	Quélet	Alkaloids	Mushroom	[65]
<i>Rhynchosia phaseoloides</i>	Ojo de cangrejo	Alkaloids	Plant	[42]
<i>Solandra brevicalyx</i>	Tecomaxóchitl	Alkaloids	Plant	[66]
<i>Sophora secundiflora</i>	Mezcal frijol	Alkaloids	Plant	[67]
<i>Stropharia cubensis</i>	San Isidro	Alkaloids	Mushroom	[68]
<i>Tagetes lucida</i>	Yauhtli	Alkaloids	Plant	[69]
<i>Turbina corymbosa</i>	Ololiuhqui	Alkaloids	Plant	[61]
<i>Turnera Diffusa</i>	Damiana	Alkaloids	Plant	[70]
<i>Ungradia speciosa</i>	Monilla	Alkaloids	Plant	[71]

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Information is shown on the alkaloid-rich main Mexican sacred plants that do not, to our knowledge, have scientific studies that evaluate their toxicity on embryo–fetal development.

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