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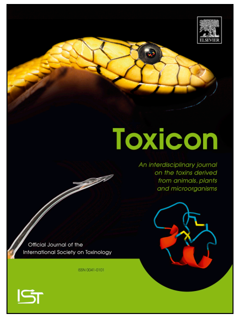


# Medicinal plants from Mexico used in the treatment of scorpion sting

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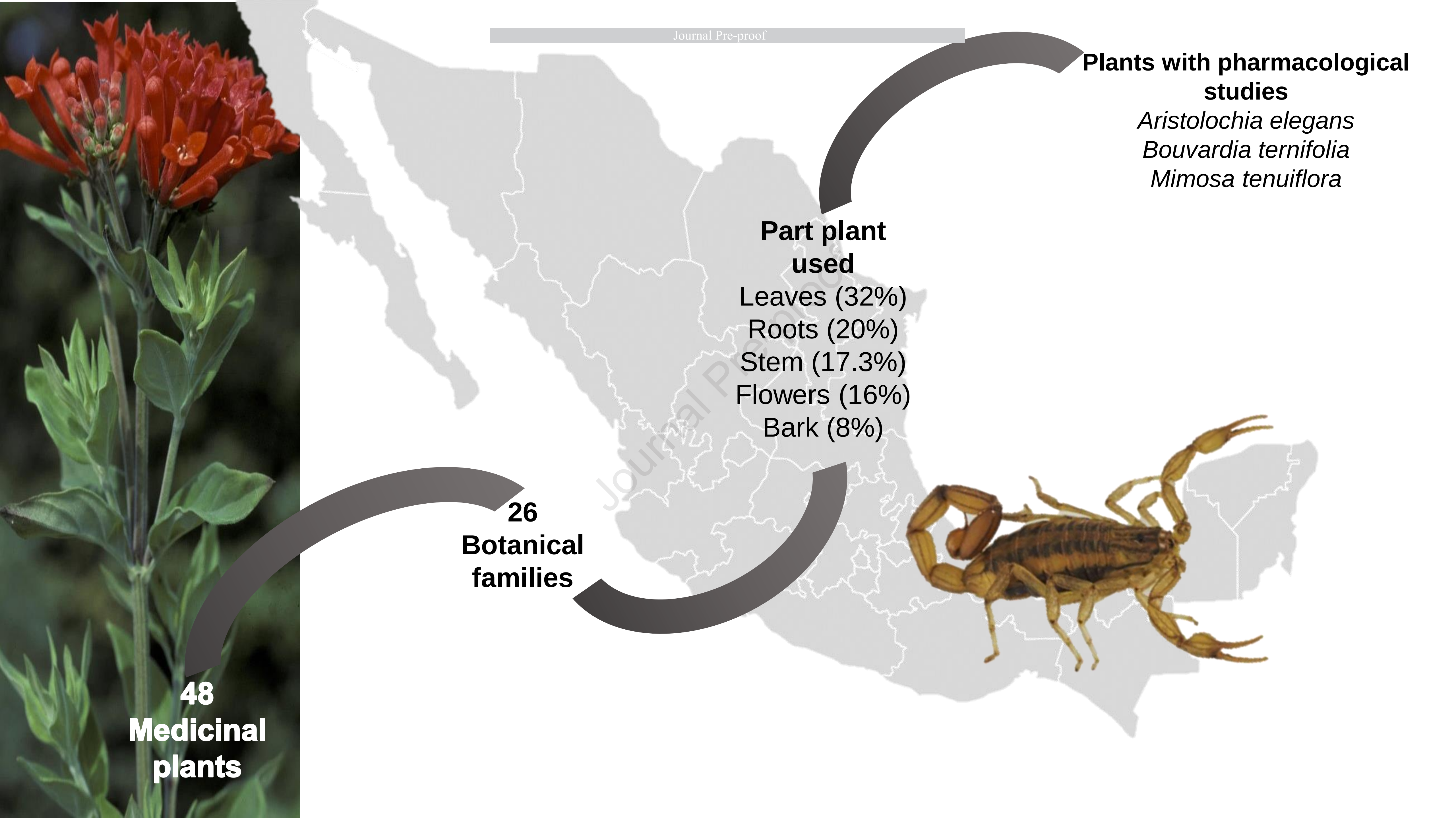
Plants with pharmacological studies
*Aristolochia elegans*
*Bouvardia ternifolia*
*Mimosa tenuiflora*
Part plant used
Leaves (32%)
Roots (20%)
Stem (17.3%)
Flowers (16%)
Bark (8%)
26 Botanical families
48 Medicinal plants

*Review Article*

**Medicinal plants from Mexico used in the treatment of scorpion sting**

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## ABSTRACT

Scorpion sting envenomation is a major public health in Mexico. Rural communities rarely have antivenoms in the health centers, therefore, the people commonly resort to using medicinal plants to treat the symptoms of envenoming caused by scorpion venom, but this knowledge has not yet been reported in detail. In this review, we carry out a review of the medicinal plants used in Mexico against scorpion stings. PubMed, Google, Science Direct, and the Digital Library of Mexican Traditional Medicine (DLMTM) were used to collect data. The results showed the use of at least 48 medicinal plants distributed in 26 families, where Fabaceae (14.6%), Lamiaceae (10.4%), and Asteraceae (10.4%) have the maximum representation. The application of leaves (32%) was preferred followed by roots (20%), stem (17.3 %), flowers (16%), and bark (8%). In addition, the most common method of use to treat scorpion stings is decoction (32.5%). The oral and topical routes of administration have similar percentages of use. *In vitro* and *in vivo* studies of *Aristolochia elegans, Bouvardia ternifolia,* and *Mimosa tenuiflora* were found, which showed an antagonistic effect on the contraction of the ileum caused by the venom of *C. limpidus*, likewise, they increased the $LD_{50}$ of said venom and even *B. ternofila* showed reduced albumin extravasation.

The results of these studies demonstrate the promising use of medicinal plants for future pharmacological applications; nevertheless, validation, bioactive compound isolation and toxicity studies are necessary to support and improve therapeutics.



## Keywords

Medicinal plants, *Centruroides*, antivenom activity, bioactive compound, *Aristolochia*

# 1. INTRODUCTION

Scorpions (class Arachnida, order Scorpiones) can survive in different terrestrial environments; therefore, it did not take them long to adapt to places occupied by humans (Stockmann, 2015). The constant interaction with people has caused an alarming increase in the number of cases of scorpion sting envenoming in various regions of the world, especially in the northern Sahara, the southern and eastern regions of Africa, the Middle East, South India, Mexico, Brazil, and the Amazonian basin area (Guyanas, Venezuela, and northern Brazil). According to some reports, there are about 1.5 million cases of scorpion stings and 3,250 annual deaths worldwide (Ahmadi et al., 2020; Chippaux & Goyffon, 2008). So far, 2, 716 species of scorpion have been reported worldwide (Rein, 2022), but only 30 species are responsible for the most deaths in the world; 29 of these species belong to the Buthidae family and one to Scorpionidae family. The scorpions of the Buthidae family are distributed mainly in the Near and Middle East (genera *Leiurus*), North Africa (genera *Androctonus* and *Buthus*), South America (genera *Tityus*), North and Central America (genera *Centruroides*), Asia (genera *Mesobuthus*) and, southern Africa (*Parabuthus*) (Chippaux & Goyffon, 2008).

Mexico harbors about 294 species of scorpions distributed in eight families (Gonzalez-Santillan & Possani, 2018; Ureta et al., 2020). To date, Mexico is the country with the greatest diversity of scorpions in the world; 21 of these species are potentially dangerous to humans and belong to the genera *Centruroides* (Gonzalez-Santillan & Possani, 2018), especially, C*entruroides noxius* which contains the most lethal venom against humans with an $LD_{50}$ of 2.5 µg per 20 g mouse (Riaño-Umbarila et al., 2016). Species of medical importance are distributed mainly along the Pacific coast and the central region.

The incidence of scorpion stings envenoming in Mexico is of the highest in the world with around 230 cases per 100,000 population, this implies that Mexican health centers and hospitals treated nearly 300,000 stings per year, even so, more than 50 deaths are reported annually (Chippaux & Goyffon, 2008).

The highest incidence occurs in Mexican Central and Pacific (Fig. 1), especially, in the population that lives in peri-urban and rural areas. These people can come to show symptoms of envenoming mild, moderate, or severe; in mild or moderate envenoming occur local pain, profuse sweating, agitation, vomiting, tachycardia, and hypertension, while in severe envenoming arrhythmia, pulmonary edema, coma, and in the worst case, death within the first 24 hours of envenoming (Ahmadi et al., 2020).

The lethality of the scorpion venom is due to toxins that affect the normal functioning of voltage-gated potassium ($K^+$) and sodium channels ($Na^+$) of excitable cells (Valdez-Velazquez et al., 2018); also, to the presence of hydrolytic enzymes (serine proteases, metalloproteases, cysteine proteases, phospholipases, hyaluronidases) that facilitate the systemic distribution of the neurotoxins from the affected tissues to the target organs. In the venom have also been detected protease inhibitors, defensins, non-disulfide bridge peptides (NDBPs), anionic peptides, superfamily CAP proteins, and insulin growth factor-binding proteins (IGFBPs), but their role during the envenoming process is still unclear (Valdez-Velazquez et al., 2018).

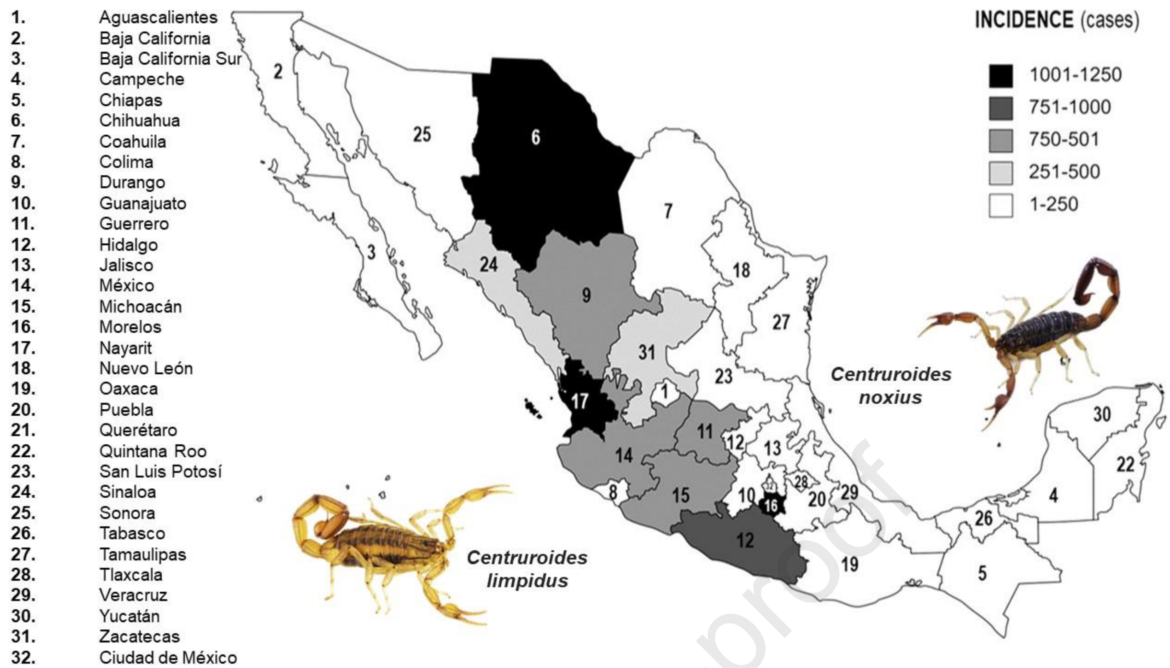


**Figure 1.** States with a higher incidence of scorpion stings in Mexico. Scorpion images from Copyright 2023, Shutterstock.

The cases of severe envenoming are managed with antivenoms (whole IgG molecules, highly purified F(ab')2 fragments, or Fab fragments) and complementary pharmacologic therapy based on the envenoming symptomatology, which is related to the scorpion lethality, the amount of venom inoculated, as well as the size, weight, age, and health of the victim (Chippaux et al., 2020). The pharmacologic treatment can include the use of antiadrenergic drugs such as prazosin, analgesics, antipyretics, anesthetics, anticholinergics, or insulin.

Despite advances in the development of antivenoms, in Mexico there are still many deaths by scorpion sting envenoming in rural communities since health centers rarely have the antivenom, this has occasioned the population to resort to the use of medicinal plants to treat the symptoms of envenoming caused by the scorpion venom. This therapeutic alternative has also been documented in other regions of the world as Egypt, Trinidad, Thailand, Jordan, India, Saudi Arabia, and the USA, even in these countries, *in vitro* and *in vivo* tests have been made to validate the antivenom properties of nine medicinal plants of family Aristolochia, Bouvardia, Barringtonia, Ambrosia, Vitex and others (Dey et al., 2013). Likewise, 68 plant species belonging to 37 families and 61 genera have been recorded in some rural communities of Pakistan, in this case, the families Solanaceae, Apocynaceae, Asteraceae, Cucurbitaceae, and Fabaceae were the most used in the treatment of scorpion stings (Shah, 2018). On the other hand, in Algerian Septentrional Sahara has been highlighted the use of the Asteraceae and Lamiaceae families between 53 plants belonging to 34 families (Telli et al., 2022).

Mexico ranks fourth in the world and third in the American continent for the diversity of vascular plants with 22,969 species, of which 12,069 are endemic (Ulloa et al., 2017). It is estimated that the population uses 4,500 species for medicinal purposes and that only 3,000 of these species are registered in the herbarium of the Mexican Institute of Social Security (IMSS). Nevertheless, only 5% have pharmacological analysis (Rodríguez-Hernández et al., 2022). Therefore, many species of medicinal plants with antivenom properties within the diversity of Mexican plants have not been disclosed.

This review describes the medicinal plants used in Mexico to treat the symptoms of intoxication by scorpion stings. In addition, the preparation methods, forms of application, and scientific studies using *in vitro* or *in vivo* models that support the antivenom properties of medicinal plants are mentioned. In the final part, some bioactive compounds and their possible mechanism of action are discussed.

## 2. METHODS

This research was carried out in PubMed, Google, and Science Direct using the keywords “Mexico, medicinal plants, scorpions, compound”. Additionally, the Digital Library of Mexican Traditional Medicine (DLMTM) was reviewed. The selection of plants was focused on their use to treat scorpion stings. Specific searches were made to enlist medicinal plant constituents and their biological activity to support the anti-venom characteristics of medicinal plants of Mexico.

## 3. RESULTS AND DISCUSSION

### 3.1 Medicinal plants used in scorpion sting treatment

In Mexico, many medicinal plants are known to treat symptoms produced by scorpion stings, but the species with only vernacular names were not considered for this review. Most of the reports were found in the database of the DLMTM. 48 medicinal plants were found to be used at various places in this country and have been enlisted in alphabetical order by family, botanical and vernacular name, state where it is used, plant parts used, and route of administration (Table 1). Possibly this number is subestimated due many plants are not listed or identified or published, so, a greater multidisciplinary effort is required to record this ethnomedical knowledge.

**Table 1.** Medicinal plants used in the treatment of Scorpion stings in Mexico.

| Family | Botanical name | Vernacular name | Place where it is used | Parts used | Mode of use | Route of administration | Reference |
|---|---|---|---|---|---|---|---|
| Acanthaceae | *Elytraria imbricata* (Vahl) Pers. | Anisillo | --- | Aerial part | Drink the infusion | Oral | DLMTM, 2022 |
| Amaranthaceae | *Teloxys ambrosioides* (L.) W.A. Weber | Epazote | North, center, and south of the Mexican Republic | Aerial part | --- | -- | DLMTM, 2022 |
| Amaryllidaceae | *Allium sativum* L. | Ajo | Huasteca potosina and Papantla | Bulb | Cataplasm of Allium sativum with *Oreganum vulgare* and *Nicotiana tabacum* is placed in the affected area | Topical | DLMTM, 2022 |
| Apocynaceae | *Thevetia thevetioides* (Kunth) K. Schum. | Yoyote | Michoacán | Seed | Cataplasm of ground seed with vaseline and apply it to the affected part | Topical | DLMTM, 2022 |

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|---|---|---|---|---|---|---|---|
| | *Asclepias curassavica* L. | Quiebra muelas | Puebla | Leaves | Cataplasm of crushed raw leaves are crushed and applied to the affected part. | Topical | DLMTM, 2022 |
| Aristolochiaceae | *Aristolochia argentea* Ule ex O.C. Schmidt | Tlacopatli | Morelos | Stem | Drink the infusion or make a maceration and spread it on the affected part | Oral or topical | DLMTM, 2022 |
| | *Aristolochia elegans* Mast. | Guaco | Morelos | Roots | --- | ---- | Jimenez-Ferrer et al., 2005a |
| | *Aristolochia grandiflora* Sw. | Chompipe | México | Roots | Drink the decoction or infusion | Oral | Hutt & Houghton, 1998 |
| Asteraceae | *Cosmos sulphureus* Cav | Chochopali | México | Flower | Decoction | Oral | Hutt & Houghton, 1998 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | *Matricaria recutita* L. | Manzanilla | Michoacán | Aerial parts (Flowers) | Boil the plant or flowers in water and administer it orally or wash the affected area | Oral or topical | DLMTM, 2022 |
| | Melampodium divaricatum (Rich.) DC. | Acahual amarillo | Nayarit | Complete plant | The plant in cooking and can be administered orally or locally | Oral or topical | DLMTM, 2022 |
| | *Lactuca sativa* | Lechuga | México | --- | --- | -- | DLMTM, 2022 |
| | *Sanvitalia procumbens* Lam. | Ojo de gallo | México | --- | Apply a cataplasm externally | Topical | DLMTM, 2022 |
| Bignoniaceae | *Tecoma stans* (L.) Juss. ex Kunth | Tronadora | North, center, and south of the Mexican Republic | Complete plant | The plant is prepared in decoction and infusion and is administered orally or locally | Oral or topical | DLMTM, 2022 |
| Burseraceae | *Bursera odorata* Brandegee | Torote blanco | Baja California Sur | Resin | Apply the resin to the affected area | Topical | Dimayuga et al., 1987 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Cactaceae | *Lophophora williamsii* (Lem. ex Salm-Dyck) J.M. Coult. | Peyote | Chihuahua and Nayarit | Aerial part | --- | Oral or topical | DLMTM, 2022 |
| Caricaceae | *Carica papaya* L. | Papaya | Guerrero | Leaves | Topical application of the maceration of the plant | Topical | DLMTM, 2022 |
| Convolvulaceae | *Ipomoea murucoides* Roem. & Schult. | Cazahuate blanco | México and Morelos | Flower, leaves, stem and bark | Administer orally the decoction of the flower, leaf, stem and bark | Oral or topical | DLMTM, 2022 |
| | *Ipomoea arborescens* (Humb. & Bonpl.) G. Don | Palo blanco | Guerrero | Bark | The bark is prepared in decoction together with other plants and applied locally | Topical | DLMTM, 2022 |
| Cordiaceae | *Cordia elaeagnoides* DC. | Cueramo | Michoacán and Guerrero | Aerial part | Drink the infusion of the plant | Oral | DLMTM, 2022 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Euphorbiaceae | *Croton ciliatoglanduliferus* Ortega | Duraznillo o mala mujer | México, Morelos and Guerrero | Complete plant (Sap) | --- | -- | DLMTM, 2022; Hutt & Houghton, 1998 |
| | *Euphorbia polycarpa* Benth. | Golondrina | Baja California Sur | Aerial part | Wash the affected part with an infusion of the plant | Topical | Dimayuga et al., 1987 |
| | *Euphorbia prostrata* Aiton | Hierba del soldado | Sonora, Nayarit, Ciudad de México, México, Michoacán, Puebla and Tlaxcala | Aerial part | Infusion | Oral | DLMTM, 2022 |
| Fabaceae | *Acacia cochliacantha* Humb. & Bonpl. ex Willd. | Cubata | México | Leaves | --- | -- | DLMTM, 2022 |
| | *Acacia farnesiana* (L.) Willd | Huizache | Nayarit and Guadalajara | Roots | Oral administration of the root infusion | Oral | DLMTM, 2022 |

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|---|---|---|---|---|---|---|---|
| | *Acacia hindsii* Benth | --- | México | Stembark | Decoction | Oral | Hutt & Houghton, 1998 |
| | *Coursetia glandulosa* A. Gray | Samota | Sonora | --- | --- | -- | DLMTM, 2022 |
| | *Erythrina coralloides* DC. | Colorín | Michoacán | Latex | Apply the latex on the affected area | Topical | DLMTM, 2022 |
| | *Leucaena doylei* Britton & Rose | Guaje de campo | Guerrero | Bark | Decoction with the bark | Oral | DLMTM, 2022 |
| | *Parkinsonia praecox* | Palo verde | Oaxaca | Bark | Drink the bark mixed with liquor or water | Oral | Rosas-López, 2016 |
| Heliotropiaceae | *Heliotropium angiospermum* Murray | Cola de alacrán | South of the Mexican Republic | --- | --- | -- | DLMTM, 2022 |
| | *Heliotropium curassavicum* L. var. oculatum (Heller) I. M. Johnston ex Tidestrom. | Alacrancillo | --- | --- | --- | -- | DLMTM, 2022 |

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|---|---|---|---|---|---|---|---|
| Lamiaceae | *Agastache mexicana* (Kunth) Linton & Epling | Toronjil | --- | Leaves | Drink the maceration of the leaves with wine or apply it on the affected area | Oral or topical | DLMTM, 2022 |
| | *Mentha piperita* L. | Hierbabuena | --- | --- | --- | -- | DLMTM, 2022 |
| | *Ocimum basilicum* L. | Albahacar | --- | Leaves | The leaves are crushed, and the paste is applied to the affected area. | Topical | DLMTM, 2022 |
| | *Vitex mollis* Kunth | Capulincillo | México, Guerrero, Michoacán, Morelos and Sonora, | Leaves | Decoction of the leaves, although it can also be applied directly to the sting area | Topical | DLMTM, 2022 |
| | *Vitex pyramidata* B. L. Rob. | Querenderenicua | Nayarit and Michoacán | Leaves | The leaves are cooked together with *Vitex mollis* and *Psidium guajava*, the resulting water is drunk frequently | Oral | DLMTM, 2022 |

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|---|---|---|---|---|---|---|---|
| Passifloraceae | *Turnera diffusa* Willd | Damiana | Baja California Sur | Branches and leaves | Decoction | Oral | DLMTM, 2022 |
| Pinaceae | *Pinus teocote* Schltdl. & Cham. | Ocote | Guerrero | Aerial part | The boiled plant is applied to the sting area | Topical | DLMTM, 2022 |
| Piperaceae | *Piper auritum* Kunth | Acoyo | --- | Leaves | The decoction of the leaf is taken, sweetened with palo honey | Oral | DLMTM, 2022 |
| Plumbaginaceae | *Plumbago scandens* L. | Cola de iguana | México | Stem and leaves | Stem and leaves are crushed and mixed, a poultice is made that is applied to the sting area | Topical | DLMTM, 2022 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Rubiaceae | *Bouvardia ternifolia* (Cav.) Schltdl. | Trompetilla | Central area of the Mexican Republic | Stem and leaves | There are different forms of application, the first is to bathe with the infusion of stems and leaves, or maceration of the leaves and stems is also applied to the affected area | Topical | DLMTM, 2022 |
| | *Coffea arabica* L. | Café | --- | --- | --- | -- | DLMTM, 2022 |
| Rutaceae | *Citrus aurantifolia* Swingle | Limón | Morelos and Guerrero | --- | --- | | DLMTM, 2022 |
| Sapotaceae | *Manilkara zapota* (L.) P. Royen | Chicozapote | --- | Bark | --- | -- | Khater et al., 2017 |
| Solanaceae | *Nicotiana tabacum* L. | Tabaco | Huasteca potosina and Papantla | Leaves | Smoke it | Inhalation | DLMTM, 2022 |

### 3.2 Distribution of plants

Medicinal plants listed in this study are distributed at various places throughout Mexico (Fig. 2), mainly in Estado de Mexico, Guerrero, and Michoacan with 6-9 medicinal plants used against scorpion venom; Baja California Sur, Jalisco, Morelos, Nayarit, and Sonora have between 3-5 medicinal plants; while Chihuahua, Sinaloa, Durango, Zacatecas, Puebla, and Oaxaca use between 1-2 medicinal plants.

There are certain similarities between the number of medicinal plants registered against this affection (Fig. 2) and the incidence of this disease (Fig. 1). It is observed that in the states with the highest incidence of scorpion stings, there is also a greater number of medicinal plants, for example, Guerrero, Michoacán, Jalisco, Nayarit.



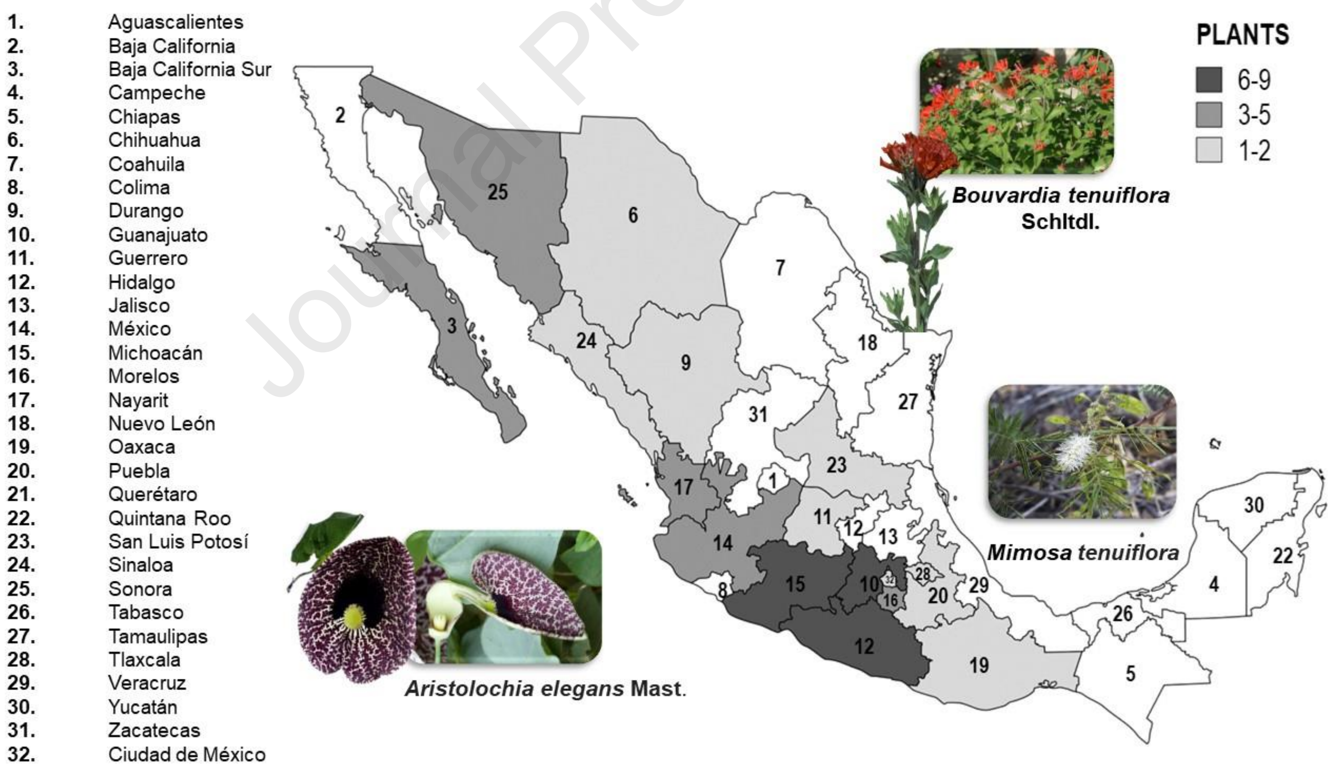


**Figure 2.** Distribution of plants used against scorpion stings. Plant images from Copyright 2023,Tropics.

### 3.3 Families more used in scorpion sting treatment

A list of 48 medicinal plants used in Mexico against scorpion stings were identified; they are distributed in 26 families, where Fabaceae (14.6%), Lamiaceae (10.4%), and Asteraceae (10.4%) have maximum representation (Fig. 3). Species from families Euphorbiaceae (6.3%), Aristolochiaceae (6.3%), Rubiaceae (4%), Heliotropiaceae (4%), Convolvulaceae (4%), Apocynaceae (4%) are also found (Fig. 3).

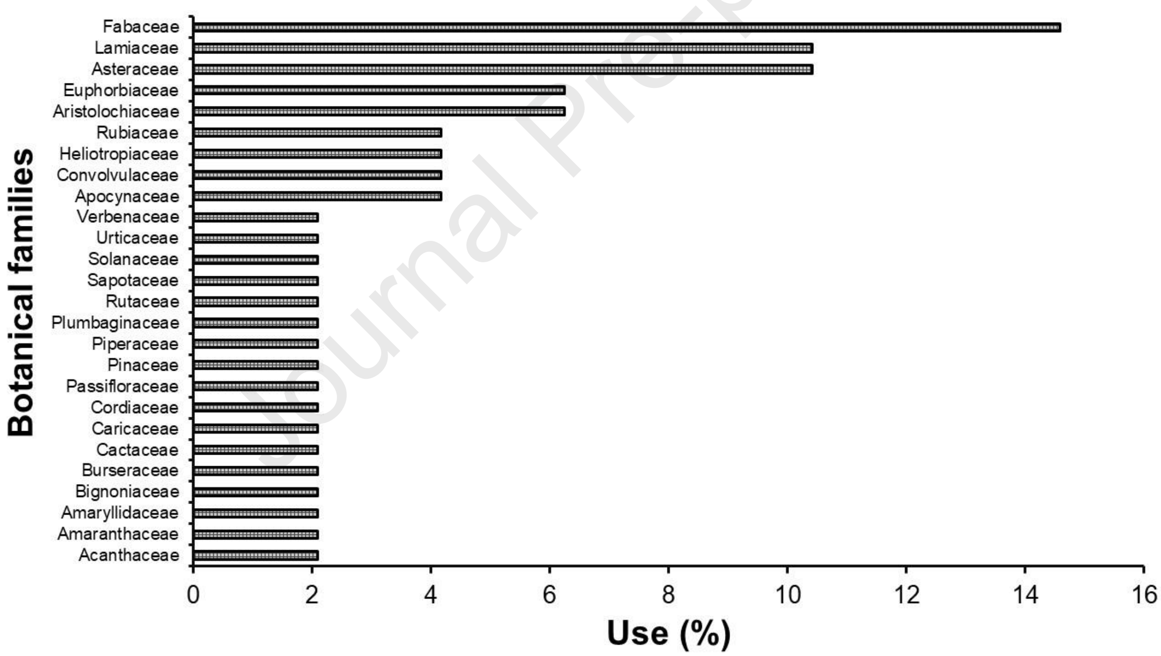


**Figure 3.** Botanical families used for the treatment of scorpion stings.

In a study carried out on Saudi medicinal plants, it was reported that the families Fabaceae (12%), Apocynaceae (11%), Amaranthaceae (9%) and Asteraceae (7%) harbor the largest number of species used against scorpion stings (Al-Asmari et al., 2017). In other countries such as Pakistan, the plants of the Solanaceae family were the most used in the treatment of snakebites and scorpion stings (Shah, 2018).

In our study *Aristolochia* (6.3%), *Acacia* (6.3%), *Ipomoea* (4.2%), *Euphorbia* (4.2%), *Heliotropium* (4.2%), and *Vitex* (4.2%) are the genera more used for the treatment of scorpion envenomation (Table 1). Hutt and Houghton (1998) reported that the genera *Aristolochia, Euphorbia,* and *Solanum* are the more used in the world for this affection. While Al-Asmari et al. (2017) reported the genera *Amaranthus*, *Heliotropium, Ipomoea, Cyperus,* and *Euphorbia* in Saudi Arabia.

Coincidences in the same genera and families suggest the presence of bioactive compounds with the same therapeutic properties in the same taxonomic group, for example, Aristolochic acid, is a common constituent of genera *Aristolochia* that inhibits the activity of phospholipases (Hutt & Houghton, 1998), which are frequently found in different venoms.

### 3.4 Plant parts and mode of use

Figure 4 shows that the leaves (32%) are the parts of the plants most used to treat the symptoms of scorpion sting envenoming. Followed by roots (20%), stem (17%), flowers (16%), and bark (8%). Other parts used are resin, latex, bulb, and branches (<2%).

Al-Asmari et al. (2017) reported the use of different parts of the plants with similar results: leaves (41%), roots (19%), whole plant (14%) and seeds (9%), latex (4%), tannin (2%), rhizome (1%) or shoot (1%). Shan et al. (2018) observed the dominant plant part was the leaf (22%).

According to mode of use of medicinal plants, the Mexican population mainly opts for the decoction (32%) and infusion (30%) methods, followed by cataplasm (25%) and maceration (13%) (Fig. 5). This trend could be because the first two methods are easier to perform and because the extracts could be used for both local and systemic application.


**Figure 4.** Parts of the plant used in the treatment of scorpion stings.

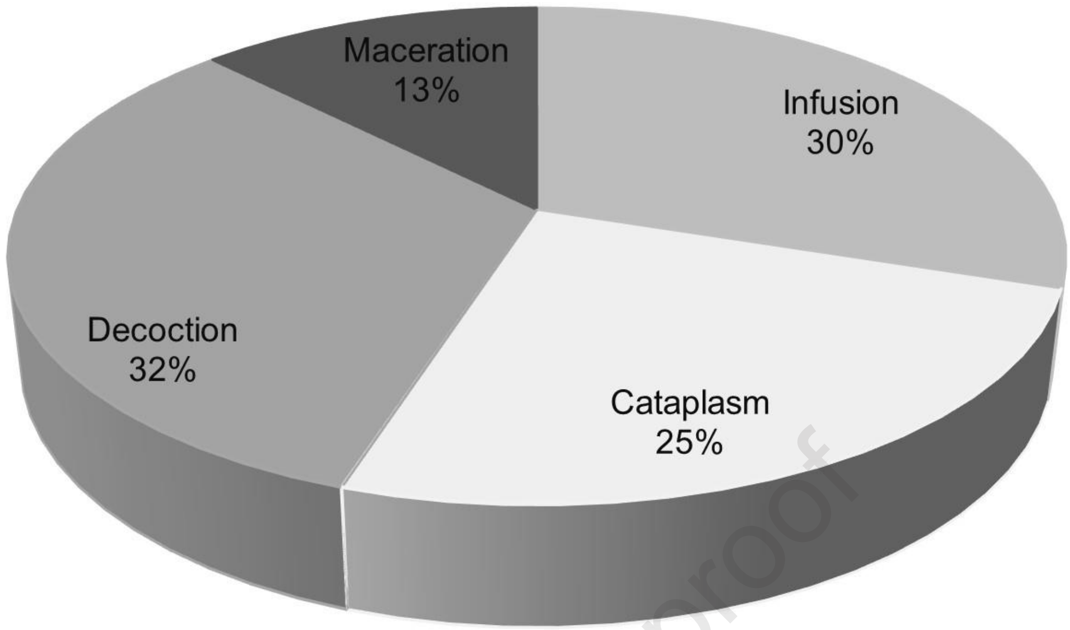


**Figure 5.** Most common modes of use of medicinal plants in the treatment of scorpion stings in Mexico.

Thus, the oral and topical routes of administration were the most common to treat the symptoms of scorpion sting envenomation (Fig. 6), both with similar percentages. In some regions of Pakistan, the cataplasm has become more popular than other application methods (Shah, 2018).

Medicinal plants used against scorpion stings may have analgesic, anti-inflammatory, and anti-pruritic effects (Hutt & Houghton, 1998), which can be local or systemic depending on the route of administration.

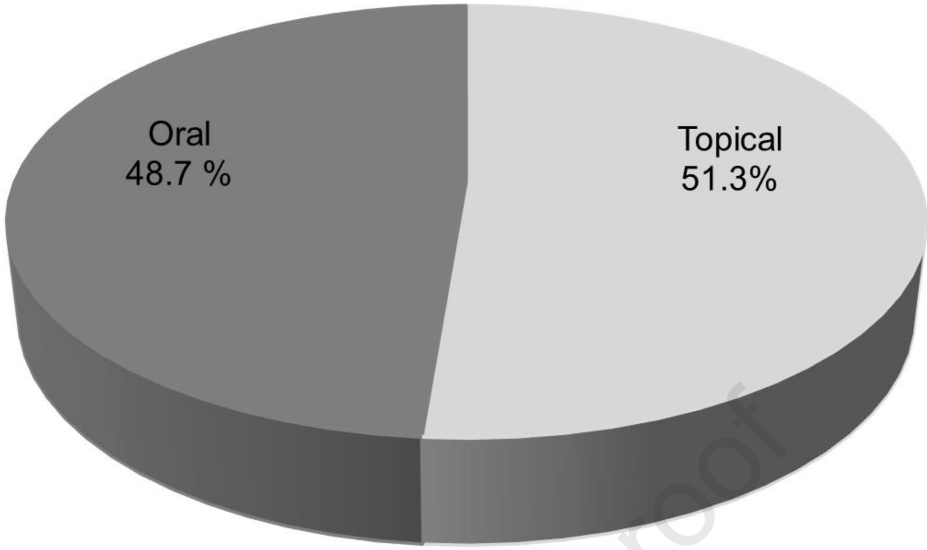


**Figure 6.** Routes of administration of the medicinal plants used in Mexico for treat the scorpion stings.

### 3.5 Studies of antivenom activity with medicinal plants and their compound isolated

Medicinal plants have played a fundamental role in diverse cultures to mitigate the effects of the sting of scorpions. In the present work, we collected data from 48 medicinal plants belonging to 26 plant families used in Mexico for the treatment of scorpion stings. Nevertheless, we found a limited number of scientific studies focused on the pharmacology of these species. Only, *Aristolochia elegans*, *Bouvardia terniflora,* and *Mimosa tenuiflora* belonging to the families Aristolochiaceae, Fabaceae, and Rubiaceae have shown anti-venom properties in animal models (Table 2). In the extracts of these plants, a wide variety of compounds have been found, mainly terpenes, alkaloids, alkenes, flavonoids, steroids, lignans, polyphenols, and alcohols were found (Table 2).

In the scientific literature, there are many reports on the pharmacological properties of the aforementioned compounds. Considering this, the medicinal plants can offer palliative effects against the symptoms of scorpion sting envenomation, since normally the effectiveness of plant extracts is lower than the commercial antivenoms (Kale et al., 2013).

We can highlight the analgesic activity of aristoquinoline from *A. elegans*, an alkaloid closely related to the antagonist activity in the nicotinic acetylcholine receptor (nAChR) (Argade et al., 2021). Likewise, it highlights the anti-inflammatory potential of Aristolactams and aristolochic acids (Desai et al., 2014), the potential of vanillin for inhibiting the expression of proinflammatory cytokines (Wang et al., 2022), and the anti-inflammatory activity of spiro-type steroids (Zhang et al., 2016). The family of terpenes has analgesic (Zielińska-Błajet & Feder-Kubis, 2020), anti-inflammatory (Lei et al., 2019), and antioxidants effects (Sharifi-Rad et al., 2018). These properties can also justify the positive pharmacological action of the extracts of *A. elegans* against scorpion sting envenomation.

**Table 2.** Anti-venom constituents from medicinal plants.

| Family | Botanical name | Isolated compounds | Extract evaluated | Experimental unit | Biological effect | Reference |
|---|---|---|---|---|---|---|
| Aristolochiaceae | *Aristolochia elegans* Mast. | Alcohols<br>Alkaloids<br>Alkenes<br>Amines<br>Aporphines<br>Aristolactams<br>Aristolochic acids<br>Bencenoids<br>Biphelyl ethers<br>Diterpenes<br>Isoquinolones<br>Lignanes<br>Monoterpenes<br>Neolignanes<br>Porphyrins<br>Steroids<br>Tetralones<br>Triterpenes | Methanolic and Hexanic extract | Guinea pig | The extracts (80 µg/mL) inhibited the contraction of the ileum by 70% when this response was induced by the venom of *C. limpidus.limpidus*. | El-Sebakhy et al., 2004; El-Sebakhy & Waterman, 1984; Jimenez-Ferrer et al., 2005a; Mix et al., 1982; Shi et al., 2004; Vila et al., 1997; Wu et al., 2000; Zamilpa et al., 2014 |
| | | | | Mice | The metanolic extract increased the $LD_{50}$ of *C. limpidus limpidus* venom from 0.750 mg/kg to 0.984 mg/kg while the hexanic extract increased the $LD_{50}$ to 1.04 mg/kg. | Jimenez-Ferrer et al., 2005a |
| Rubiaceae | *Bouvardia ternifolia (Cav.) Schltdl* | Triterpenes<br>Polifenols<br>Coumarines<br>Bicyclic hexapeptides | Methanol extract<br>Hexane extract | BALB/c mouse<br>Sprague-Dawley rats | Albumin extravasation wasreduced by 60% when induced by *C. limpidus* venom. | García-Morales et al., 2015; Jiménez-Ferrer et al., 2005a |
| | | | | Mice | The metanolic extract increased the $LD_{50}$ of *C. limpidus limpidus* venom from 0.750 mg/kg to 1.16 mg/kg while the hexanic extract increased the $LD_{50}$ to 1.64 mg/kg. | Jimenez-Ferrer, 2005a; Jolad et al., 1977 |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | Guinea pig | The extracts (40 μg/mL) inhibited the contraction of the ileum by 70% when this response was induced by the venom of *C. limpidus limpidus*. | Jimenez-Ferrer, 2005a |
| Fabaceae | *Mimosa tenuiflora* | Phenoxychromones<br>Alkaloids<br>Saponins<br>Steroids<br>Alcohols<br>Aromatics<br>Amines | Aqueous extract | Male BALB/c mice | Reduction in leukocyte migration to the peritoneal cavity. Reduction in the level of proinflammatory cytokines IL-6, IL-12, IL-1β | Amariz et al., 2022; Gardner et al., 2014; León et al., 2004; Oliveira et al., 2014 |

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On the other hand, the compounds identified in *Bouvardia terniflora* could be related to the decrease in mortality of mice affected by *C. limpidus* venom and to the inhibition of smooth muscle contraction in the ileum of guinea pigs (Jimenez-Ferrer et al., 2005). In a study was determined that methanolic and hexanic extracts from the roots of *B. terniflora* are responsible for the inhibition of albumin extravasation in rat pancreas caused by the *C. limpidus venom.* This secretagogue effect was verified by isolating pancreatic amylase in a dose-dependent manner after exposing the pancreas of mice to *C. limpidus* venom. The properties can be attributed to the presence triterpenes, polyphenols, coumarins and hexapeptide bicycles (García-Morales et al., 2015; Jiménez-Ferrer et al., 2005; Jolad et al., 1977).

Finally, the aqueous extract of *M. tenuiflora* demonstrated a reduction in the migration of leukocytes to the peritoneal cavity, which reduced the levels of proinflammatory cytokines in mice inoculated intravenously with *Tytius serrulatus* venom. Of this plant species has been reported the presence of chromones, alkaloids, saponins, steroids, alcohols, and aromatic compounds (Amariz et al., 2022; Gardner et al., 2014; León et al., 2004).

The compounds above mentioned presented a wide variety of pharmacological effects, however, cannot be considered antivenom, but the palliative effect against the main symptoms can be inferred against scorpion sting envenoming. On the other hand, the antivenom activity of a plant could be attributed to the mixture of active compounds; which can have a synergistic effect on different targets such as enzymes and receptors.

## 4. CONCLUSIONS

This review demonstrates that herbal remedies play an important role in scorpion sting treatment, especially in rural communities where health centers rarely have antivenom available. In such instances, herbal therapeutics seems to be a viable alternative. There is a need to create centers or organizations that cultivate medicinal plants with anti-venom properties to exploit the knowledge hidden in traditional medicine and preserve this knowledge for future generations. Evidently, to apply this knowledge, first one needs to isolate and characterize the active compounds. Extensive research on the mechanism of action of these compounds at the biochemical and molecular level is also required to demonstrate their prophylactic efficacy in *in vivo* and *in vitro* models. In addition, further studies are required focused on enhancing the action of antivenoms with a complementary therapy based on the use of plant extracts or pure compounds. It is also important to establish *in vitro* plant propagation methods to avoid overexploitation of medicinal plants.

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# Highlights

- Number of medicinal plants registered to treat scorpion stings is according to the incidence of this disease.
- *A. elegans, B. ternifolia,* and *M. tenuiflora* decreased proinflammatory cytokines and $DL_{50}$ of *Centruroides sp.*
- Triterpens, polyphenols, coumarins, and hexapeptide cycles of plants could be responsible for the antivenom effect.

**Ethical Statement**

There are no animal or human subjects in this article and informed consent is not applicable.

**Declaration of interests**

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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