

**REVIEW**


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**SPIDERS IN BRAZIL: FROM ARACHNIDISM TO  
POTENTIAL THERAPEUTIC USE OF THEIR VENOM**

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**PART 1 OF 2**

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**ABSTRACT**

Spider envenomation, generically known as arachnidism, is described in many places around the world. In terms of medical importance, the following genera of animals stand out as the main origin of the morbid condition: *Atrax* (Sidney funnel web spider), *Steatoda* (false black widow), *Latrodectus* (black widow), *Loxosceles* (brown spider) and *Phoneutria* (armed spider), the last three causing accidents involving spiders in Brazil. This article, part 1 of 2, aims to present the main aspects of arachnidism in the country, with an emphasis on the biology and geographical distribution of spiders, biochemistry of the venom, pathogenesis and epidemiology of arachnidism, as well as prevention of the morbid condition.

**KEY WORDS:** Arachnidism; araneae; spider bites; spider venoms.

**INTRODUCTION**

Spiders are invertebrate animals that belong to the phylum Arthropoda, class Arachnida and order Araneae (Brazil, 2021). This group of living beings consists of 49,657 species (<https://wsc.nmbe.ch/>), the majority of which are venomous since they have toxin-producing glands and an inoculating device, used to inject the venom during prey capture or for defense against predators (Foelix, 2011).

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Received for publication: 27/1/2021. Reviewed: 24/9/2021. Accepted: 7/3/2022.

Spider envenomation is referred to as arachnidism and was responsible for almost 400 thousand cases between 2000 and 2017 throughout Brazil (Brazil, 2018). The toxins can cause pain, necrosis, organ failure and even death (Haddad et al., 2012). Furthermore, the severity of each accident is closely related to the chemical nature of the toxins produced by each spider, which are sometimes complex substances formed by enzymatic compounds, polyamides and other components, capable of binding to ion channels and receptors and altering their activity (Saez et al., 2010).

Some genera of spiders are clinically and epidemiologically harmful to humans, particularly in accidents caused by *Atrax* (Sidney funnel web spider), *Latrodectus* (black widow), *Loxosceles* (brown spider), *Phoneutria* (armed spider) and *Steatoda* (false black widow). Specifically in Brazil, the genera *Loxosceles*, *Phoneutria* and *Latrodectus* (figures 1, 2 and 3, respectively) are of the greatest medical importance as they are responsible for most of the accidents (Isbister & Framenau, 2004; Cordeiro et al., 2015; Arán-Sekul et al., 2020).

Based on these summarized considerations, this article (part 1 of 2) aims to present a narrative literature review “*that describes and discusses the state of the science of a specific topic or theme from a theoretical and contextual point of view*” and that “*consists of critical analysis of the literature published in books and electronic or paper-based journal articles*” (Rother, 2007, p. 2); regarding the species of spiders of medical importance as well as the biochemical composition of their venom, focusing equally on the pathogenesis, epidemiology and prevention of arachnidism.

## SPIDER BIOLOGY

Most species of the order Araneae have an inoculating apparatus and glands that produce toxins used to capture prey or for defense against predators, thus being classified as venomous spiders (Brazil, 2021; Langenegger et al., 2019; Pennisi, 2017; Santana et al., 2020a; Santana et al., 2020b). Table shows the taxonomic classification of the main spiders responsible for accidents involving humans in Brazil (Figures 1, 2 and 3).

A spider’s exoskeleton is composed of chitin and its body is divided into cephalothorax and abdomen. The cephalothorax, or prosoma, presents six pairs of articulated appendages, one with chelicerae (venom inoculating structures), one with pedipalps and four legs, as well as eyes, which can vary in number, from zero to eight (Foelix, 2011). In the abdomen — or opistosome — which is shaped like a bag, are the respiratory and reproductive openings, the anal orifice and, in general, two or three pairs of spinnerets (appendages with glands related to silk production) (Freitas, 2011).

Table. Taxonomic classification of spiders of medical importance in Brazil: *Latrodectus*, *Loxosceles* and *Phoneutria* genera.

Animalia (kingdom)  
Ecdysozoa (superphylum)  
Arthropoda (phylum)  
Chelicerata (subphylum)  
Arachnida (class)  
Araneae (order)  
Opisthothelae (suborder)  
  
Theridiidae (family)  
*Latrodectus* (genus)  
Sicariidae (family)  
*Loxosceles* (genus)  
Ctenidae (family)  
*Phoneutria* (genus)

Sources: U. S. National Library of Medicine - NCBI Taxonomy  
Arctos – Collaborative Collection Management Solution



*Figure 1. Loxosceles* (brown spider).  
Image prepared by Prof. Ademir Nunes Ribeiro Júnior (FADIP).



*Figure 2. Phoneutria (armed spider).*

Image prepared by Prof. Ademir Nunes Ribeiro Júnior (FADIP).



*Figure 3. Latrodectus (black widow).*

Image prepared by Prof. Ademir Nunes Ribeiro Júnior (FADIP).

Spiders are carnivorous and feed mainly on insects, playing a relevant role in the control of these invertebrates contributing to the ecological balance. They are also prey within the food chain, serving as sources of nutrition to various animals, such as birds, geckos, frogs and even other spiders, (Freitas, 2011; Koltz & Wright, 2020). Furthermore, mites and wasps (the latter lay their eggs on the arthropod's surface) can be spider parasites.

From a reproductive point of view, spiders are oviparous. The female usually lays her eggs once a year — the number varying from a few dozen to more than a thousand — in a wrapping of intertwined silk threads which is called an ootheca (Trabalon et al., 2018; Freitas, 2011). This structure is taken care of by the female spider. Males, according to Bertani et al. (2015), reach sexual maturity by going through the last ecdysis, the exoskeleton change process and animal growth, when the last segment of the palp is transformed into a copulatory organ, the so-called copulatory bulb, whose complexity depends on the group to which the species belongs. This organ is used by the animal in its reproductive process (storage of sperm and copulation) (Bertani et al., 2015; Dederichs et al., 2019). Due to the rigidity of the arthropod's cuticle, it is the successive ecdyses that allows it to grow to adulthood and, in some cases, can occur throughout the spider's life cycle.

The arachnid's body can be infected by several microorganisms and at the time of ecdysis these arthropods can lose hemolymph, a fluid that has antimicrobial molecules, including migaline (Espinoza-Culupú et al., 2020), a molecule related to ROS (reactive oxygen species) generating mechanisms and chelation of iron ions, which are necessary for bacterial metabolism.

Most spiders are terrestrial, except the *Argyroneta* genus, which manages to remain underwater for extended periods, given the animal's ability to store oxygen in its hairs (Correa-Garhwal et al., 2019). Life expectancy of spiders varies; in fact, while some species live for only a few months, others can live for more than 20 years (Freitas, 2011).

## SPIDERS IN THE WORLD

Although there are thousands of spider species worldwide, not all species pose risks for *Homo sapiens*. In some cases, accidents involving these animals can evolve with significant severity, constituting a real threat to the patient's health.

Spiders of the genus *Atrax* are responsible for severe accidents as their neurotoxic venom is potentially lethal (Herzig et al., 2020). Most of the morbid conditions result from male bites, since these are more aggressive and venomous than females (Harrington et al., 1999). Spider bites may cause severe systemic reactions that can mimic organophosphate poisoning. Among the species of this genus, *Atrax robustus* or the funnel web spider is the most important; its name comes from the construction of tapered spiral webs (Silva,

2015). The species is found especially in northern Australia and the forest regions in Tasmania (Silva, 2015), which is why it is also referred to as the Australian spider.

*Loxosceles* spp. can be found in temperate and tropical regions, predominantly in North, Central and South America and Africa. Spiders belonging to this genus build their webs, which are usually irregular, away from light and in human homes, especially indoors (behind furniture and paintings; in clothing and footwear) and in external areas (bark, debris and stacked bricks) (Brazil, 2001). In addition, brown spiders are not aggressive, but because they take shelter inside peoples' homes and take refuge in pieces of clothing, they end up causing accidents when compressed against the human body (Brazil, 2001). Accidents caused by spiders of this genus are called loxoscelism and the main species responsible for these accidents, in Brazil, are *Loxosceles intermedia*, *Loxosceles laeta* and *Loxosceles gaucho* (Malaque et al., 2002; Gonçalves et al., 2003; Lucas, 2003). These spider bites evolve with local necrosis, although this occurs in few cases (Lopes et al., 2020).

*Phoneutria* are found in South and Central America. Spiders of this genus are aggressive and when attacking raise both pairs of anterior legs, justifying the popular name armed spider, as they are called in most of Brazil (Simó & Brescovit, 2001). Spider bites pertaining to this genus are painful and like bee stings (Bucaretschi et al., 2008). Their venom resembles that found in scorpions of the genus *Tityus* and may have similar effects (Santana et al., 2020c).

Among the spiders of the *Latrodectus* genus, females threaten human health. These are small and have a globular abdomen (Brazil, 2003; Khamtorn et al., 2020). They are found in tropical and subtropical areas of the world (Lirada-Silva et al., 1995), where they usually inhabit shrubs and grassy vegetation, but they may also have household and peridomestic habits (Brazil, 2003).

Lastly, the species *Steatoda nobilis* — or false black widow — belongs to the same family as the spiders of the *Latrodectus*, Theridiidae. Although they are found worldwide, these spiders do not frequently cause accidents involving humans, when compared to other spiders. In addition, the signs and symptoms of these accidents are much less severe when compared to those caused by legitimate black widows (Dunbar et al., 2022). According to Borges (Borges et al., 2008), this species of spider is abundant in low altitudes and areas with natural forest vegetation. *Steatoda* is also common in urban areas, often found indoor, where solid waste abounds, as it is a web-building species (Abbasi et al., 2019). Furthermore, they are often detected in banana trees (Borges et al., 2008).

The genera of medical importance mentioned above include a relevant number of species, namely: 141 *Loxosceles*, 121 *Steatoda*, 32 *Latrodectus* and nine *Phoneutria*.

## SPIDERS IN BRAZIL

The number of spider species described in Brazil is approximately 4,000 (four thousand), but only three genera are of great medical importance in the country: *Latrodectus*, *Loxosceles* and *Phoneutria* (Brazil, 2021; Hickman et al., 2004). However, *Lycosa* genus (grass spider) are also relevant, despite the toxicity of their venom being insignificant (Isbister & Framenau, 2004).

*Latrodectus* are known both for the fact that the female feeds on the male after copulation, as well as for their colors (Peterson, 2006). They are small - measuring about 3 cm - and one of the characteristics of some specimens is the presence of a reddish design on the lower part of the abdomen, in the shape of an hourglass (observed in *L. mactans*). The venom of the Brazilian black widows is much less toxic than that present in European species (Fusto et al., 2020). Thus, in Brazil, there are few cases considered severe and they are often associated with sensitivity to spider bites. In addition, these accidents are not frequent and are seen mostly in the states of Minas Gerais, São Paulo, Bahia and Pernambuco (Brazil, 2021).

*Loxosceles* have a greenish brown coloration and their body rarely exceeds three centimeters (Santana et al., 2020a). It is a genus of domestic spiders, whose web resembles a “cotton ball”. Many harmless spiders look and live in the same places as the brown spider, but only a specialist is able to tell the difference between them. These arthropods are not aggressive, have sedentary and nocturnal habits, and accidents usually occur from October to March (Foelix, 2011). *Loxosceles* proved to be the main spiders involved in the 1,126 accidents between 1994 and 2006 in Criciúma, Santa Catarina State, Brazil (Cristiano et al., 2009).

*Phoneutria*, in turn, are among the most aggressive spiders in the world; in fact, they stand on their hind legs and jump on the victim or predator. They have nocturnal habits and do not have permanent dwellings, being known to enter houses during the night and hide in footwear, causing accidents (Lucas, 2015). Most attacks occur between January and May mainly in the Southeastern, Southern and Northern regions (Amazon) of the country (Brazil, 2001).

Spiders of the *Lycosa* genus can be incorrectly identified, as they are spiders that have a similar method of defense, raising their front legs when intimidated (Brazil, 2014). They are wandering animals, with diurnal and nocturnal activity and are common in urban areas, mainly in lawns and gardens (Engel et al., 2020). They have an arrow design on the dorsal part of their abdomen and measure 3 to 5 cm. Their bite is painful, but the venom of these arthropods does not pose great threat to human health, causing transient pain, redness and edema (Wolfart et al, 2009).



## BIOCHEMISTRY OF THE VENOM AND PATHOGENESIS OF ARACHNIDISM

Spider venoms are complex, and several identified molecules have been studied for their use in the composition of biotechnological products that can be utilized by the pharmaceutical industry or for agricultural purposes such as pest control (Saez et al., 2010; Herzig et al., 2020). Although still unclear, the components of the venom of these invertebrates are an unexplored treasure trove of active biological compounds (Peigneur et al., 2018). Toxins derived from arthropods — mainly spiders and scorpions — are a little-known source of new biologically active molecules, such as proteins and other non-protein substances, with promising scientific applications (Bonfanti et al., 2020).

Spider venoms, in general, have peptide components and their compositions vary according to taxa. The inoculation of toxins produced by some of these animals causes several consequences, ranging from inflammation and symptoms such as pain, heat, erythema and edema, to necrosis, organ failure (mainly kidneys) or death (Haddad et al., 2012; Erat et al., 2020). In general, a few hours after venom inoculation inside the body, hemolysis and activation of the complement system occur, triggering the inflammatory response process since the venom consists of enzymes that act in the cellular membranes, commonly in endothelial cells. With the inflammatory process initiated, edema appears, followed by obstruction of local blood capillaries, hemorrhage and possible tissue necrosis (Cupo et al., 2003).

The compounds produced by *Loxosceles*, for example, have mainly dermonecrotic and hemolytic action, the inoculation of which can cause cutaneous or cutaneous-visceral (hemolytic) manifestations. Among toxic and enzymatic substances, collagenases, sphingomyelinase-D, alkaline phosphatase, hyaluronidases, lipases, metalloproteases and peptidases can be highlighted, in addition to various inorganic components such as calcium and sodium (Fernandes-Pedrosa et al., 2008). Sphingomyelinase-D is able to catalyze the hydrolysis of sphingomyelin, trigger reactions that involve the complement system and promote the migration of polymorphonuclear cells, platelets and endothelial cells, therefore considered the main component in the generation of dermonecrotic lesions. The enzyme is also responsible for the impairment of blood irrigation by facilitating the formation of microthrombi, which can culminate in ischemia in organs such as the liver and kidneys (Tambourgi et al., 1998). Hyaluronidases and proteases, in turn, are involved in the dissemination of the venom throughout the organism since they allow it to penetrate the tissues (Ferrer et al., 2013). Metalloproteinase is a component related to hemorrhage, disseminated intravascular coagulation and destruction of fibrinogen and fibronectin (Feitosa et al., 1998; Santana et al., 2020a; Santana et al., 2020b). Renal failure can occur not only due to the formed microthrombi, but also due to hemolysis, hemoglobinuria and glomerular



disorders that result from lesions in the glomerular basal membrane. Venoms also have protein neurotoxins, several complex polyamides or acyl polyamines and non-protein neurotoxins that promote postsynaptic receptor inhibition. Some of these components, such as peptide toxins, when they encounter cell receptors, in particular ion channels (sodium, potassium and calcium channels) modify their activities (Saez et al., 2010).

The venoms of *Phoneutria* are complex and cause a number of local sequelae, ranging from intense pain and spastic paralysis to systemic changes, including autonomic dysfunction, seizures, priapism, tachycardia, visual disturbances, fasciculation, pruritus and death. The toxins produced by this genus include histamine, serotonin, hyaluronidase, proteolytic enzymes, as well as a variety of proteins and peptides, including neurotoxins that act upon ion channels (Santana et al., 2020a). The neurotoxic action of the venom is related to its effects, mainly, on the sodium channels, promoting the depolarization of the sensitive, muscular, motor and autonomous nerve endings, thus favoring the release of neurotransmitters, mainly acetylcholine and catecholamines, which induce the systemic alterations mentioned above (Araújo et al., 1993; Peigneur et al., 2018). It is worth mentioning that these peptide toxins are used against a wide variety of pharmacological targets, making them important agents in research on properties of pharmacological receptors in different experimental paradigms (Souza, 2013).

Another venom of medical relevance is that of the black widow and other species of the genus *Latrodectus*. Alpha-latrotoxin ( $\alpha$ -latrotoxin) is the main toxic component produced by these spiders (Keyler et al., 2020). This substance targets sensitive nerve endings, causing severe pain in the affected region and engendering the release of adrenergic and cholinergic neurotransmitters that, upon reaching the presynaptic neuromuscular junction, distort sodium and potassium ion permeability (Brazil, 2001).

## ARACHNIDISM EPIDEMIOLOGY

Few of the almost 50 thousand species of spiders in the world do not present venom. However, due to the fragile oral apparatus and the small size of these animals, most are not able to cause harm to *H. sapiens*. Nonetheless, arachnidism is not only a clinical problem, but also a significant public health issue. Since the colonial period, accidents caused by spiders have been reported in Brazil (Martins et al., 2011). Starting in the second half of the 1980s, there has been progress in recording arachnid morbid events (Sinitox, 2011). However, in certain regions of Brazil, such as in the Northeast, records of spider accidents are scarce and possibly underestimate the true risk situation in the area (Brazil, 2021). Underreporting and the lack of recognition of the real dimension of this problem generally occurs throughout the country (Lemos et al., 2009).

In Brazil, there has been an increase in the number of cases of arachnidism — and related deaths — in recent years (figures 4 and 5). Annually, an average of 20,000 cases of spider accidents are recorded in the country, 90% of which occur in the South and Southeast (Barbosa, 2015). Nationally, as mentioned, *Latrodectus*, *Loxosceles*, and *Phoneutria* are the genera with the greatest medical relevance, being responsible for approximately 81% of accidents (Cordeiro et al., 2015; Martins et al., 2011). However, there are occurrences related to other genera already mentioned, such as *Lycosa* and *Grammostola* (Bucherl, 1969; Diefenbach et al., 1969).

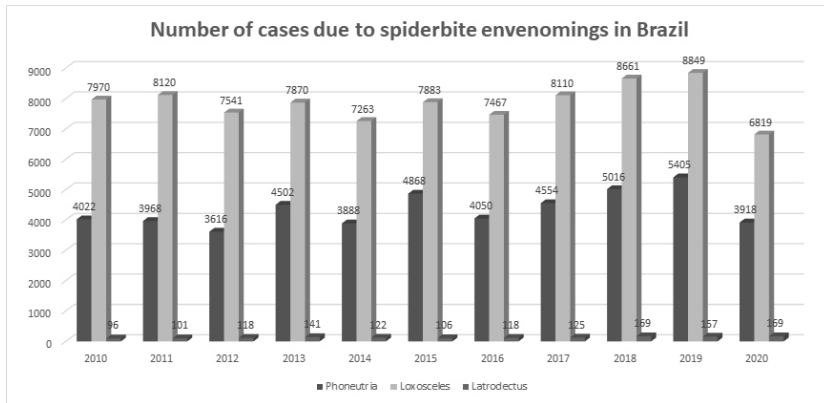


Figure 4. Number of cases of arachnidism in Brazil (2010-2020).  
Source: DATASUS.

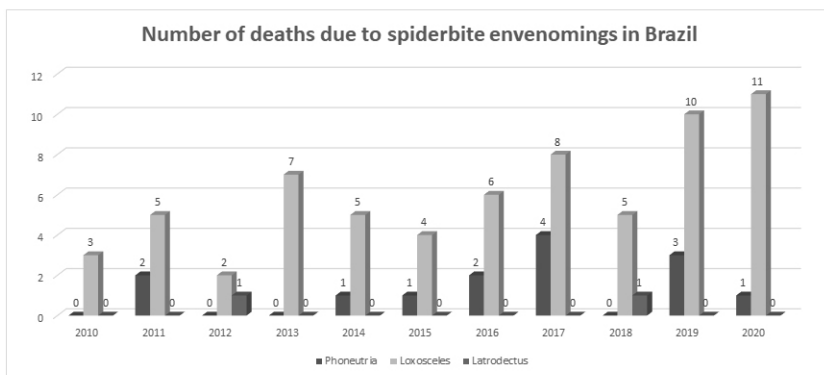


Figure 5. Number of deaths by arachnidism in Brazil (2010-2020).  
Source: DATASUS.

The most important form of arachnidism in Brazil is due to *Loxosceles* bites, a clinical condition therefore referred to as loxoscelism, this spider is responsible for most accidents, which usually occur in young adults, close to 30 years of age. Morbid events are more common in the countryside, habitat of most species of spiders, which shelter under foliage, stones and logs and in tree bark (Silva, 2015). The prognosis is generally good (Brazil, 2001; Brazil, 2021). In accidents involving *Phoneutria* specimens, deaths are rare, with 14 deaths described in the national literature from 1926 to 1996. However, it is important to keep infants, preschoolers and the elderly under observation for at least six to 12 hours after the accident. The cases involving *Loxosceles*, on the other hand, can be more severe, concomitant with intravascular hemolysis; in many cases, skin lesions of difficult and lengthy cicatrization can occur (Nguyen & Pandey, 2019). The prognosis of latrodectism is satisfactory, considering that deaths as very rare events (Santana et al., 2020a).

The treatment of arachnidism will be presented in part 2 of 2 of this article.

## PREVENTION

Accidents caused by spiders are avoidable. In general, cleaning the house and its surroundings regularly with emphasis on attics, basements, garages, backyards and other similar areas, is considered one of the most important control measures. Keeping these sites free from the accumulation of materials that can become potential hiding places for arachnids minimizes the risk of accidents. Another feasible approach refers to the breeding of certain birds, which are natural spider predators (Silva et al., 2005).

The search for food and sexual partners is a stimulus for spiders to enter buildings; therefore, shoes, clothes, corners of domestic rooms and accumulated waste (inside and outside the home) can become the perfect hiding places for these animals. Whenever possible, checking for spiders in these places — for example, before putting on shoes and drying yourself with a towel is advisable to avoid accidents (Brazil, 2003).

However, once an accident has occurred, it is crucial to know what species of spider was the cause. For this reason, it is important to remain calm and observe its morphological characteristics (or photograph it), if possible. If the spider has been captured, it should be taken to the emergency room, where a complete assessment of both the patient's symptoms and signs and the arachnid will be made (Cabrerizo et al., 2009). Before proceeding with any type of treatment, the doctor must make a complete anamnesis analyzing all the information regarding the accident and a thorough physical examination, regardless of whether the spider has been identified or not (Ramos et al., 2015).

In recent years, some efforts have been made to develop vaccines for arachnidism prophylaxis, especially for *Loxosceles* (de Moura et al., 2011; Oliveira et al., 2016). These works, although preliminary, are promising.

## FINAL CONSIDERATIONS

The purpose of this article, part one of two, was to address arachnidism, dealing with several aspects related to the subject, covering the main spiders that cause accidents involving humans, focusing on their biological aspects, the pathophysiology and epidemiology of the morbid condition. Furthermore, the study sought to elucidate and distinguish the action of the main bioactive constituents that make up spider venom, the importance of prophylaxis and the control of arachnidism. The relevance of recognizing, whenever possible, the spider that caused the accident is also important as this may help in the analysis of clinical manifestations and case management, as will be discussed in the next article.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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