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Necrotic Araneism. A Review of the *Loxosceles* Genus. I. General Aspects, Distribution and Venom Composition

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Abstract: The "violin" spider, *Loxosceles sp* is implicated in causing necrotic skin lesions, secondary complications and in some instances, even considered life-threatening. Fatalities are rare but are much more common in children, the ill and the elderly. Diagnosis is often made by examining the lesion after the bite and rarely is a spider identified at the time of the attack. The "fiddle back" spider is distributed extensively in Mexico, with the majority of the species living in the Northern states. These spiders have a preference of hiding in closets, boxes, waste material, under rocks and in crevices and are considered "synanthropic".

Key words: Arachnidism · *Loxosceles* · necrotic arachnidism · necrotic ulcer · "Violin" spider · venomous spiders · spider envenomation

INTRODUCTION

The first representatives of the Arachnidea class appeared in the Silurian period of the Paleozoic era, over 360 million years ago. After acquiring aquatic habits, they reached their maximum development during the Carbonipherous period of the same era, approximately 300 million years ago. It is during this period when they became terrestrial. The current species appeared during the Cenozoic era, 60 million years ago (Table 1) [1, 2].

Spiders, just as scorpions, are important to the public health sector since their bites are often harmful to adults [5]. They use their venom to kill insects and as a defense mechanism [6, 7], but considering their dimensions, the amount of the inoculums and how fragile their oral organs are, it is rare for them to cause severe lesions in subjects [8, 9]. Nonetheless, of the more than 50,000 known species recognized worldwide, only 180 of them (0.45%) defend themselves aggressively and have chelicerae large enough to penetrate the human skin [10, 11, 14]. The species of greatest medical importance in the American continent are the "black widow" (*Latrodectus mactans*) and the "brown" (*Loxosceles sp*) [8, 12]. In fact, the World Health Organization considers four genera of spiders to be of real medical interest due to the clinical manifestations them cause and the lethality of their venom, three of them belonging to the infraorder Araneomorphae: *Latrodectus*, Theridiidae family; *Loxosceles*, Loxoscelidae family; *Phoneutria*, Ctenidae family. The fourth genus belongs to the Mygalomorphae infraorder (Atrax, Hexathelidae family) [13]. They are shy animals, never aggressive and only inflict bites when threatened, if violently touched or when pressed, almost always accidentally (70% during the night) [14-16]. One must remember, that spiders do not attack in groups, do not wait in lieu of becoming aggressive and some may even jump, but not intentionally attacking humans [17].

Table 1: Taxonomy of the *Loxosceles* genera spider [3, 4]

Kingdom	Animalia
Phylum	Arthropod
Subphylum	Chelicerata
Class	Arachnid
Order	Araneae
Suborder	Labidognatha
Infraorder	Araneomorphae(real spiders)
Family	Sicariidae (Loxoscelidae)
Genus	*Loxosceles*
Species	*Loxosceles sp*

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The incidence is unknown, but it is thought that females are more affected and attacks usually occur in children [9, 14, 18]. Cases of intoxication by the venom of the *Loxosceles* in template zones of Europe, Africa, Australia, Asia and America have been recorded, each year registering an important number of cases of intoxication due to spider bites. In México, these observations were recorded in the states of Jalisco, Michoacán, Sinaloa, Sonora and Guanajuato as those of greatest incidence [19, 20]. Some species are endemic, such as *L. tehuana*, unique to Oaxaca and Puebla [21]. In fact, close to 300,000 doses of sera are administered annually to save the lives of people that are stung or bitten by scorpions, snakes and black widow spiders [22, 23]. Surely, the exposure to the *Loxosceles* venom can be mortal, be the cause of absenteeism from work for several weeks or leave important secuelae from an esthetic standpoint [24].

It is the second most frequent spider to cause accidents in countries such as Mexico and Peru [25].

Epidemiology: Loxoscelism was first described in 1872 when Chilean physicians associated a peculiar skin lesion known as "a gangrene ulcer from Chile" or "gangrene in flame" to bites from *Loxosceles laeta* [26, 27]. In the United States, *Loxosceles recluse* was the first spider related to necrotic arachnidism (named by some as chronic arachnidism [28] in 1957 [29, 30]. In 1984, at least five deaths were reported [31]. Nonetheless, severe cases started occurring at the end of 1800 and currently in endemic areas, this spider continues to be of clinical importance [32]. *L. laeta*, that produces more severe reactions than *L. deserta*, was imported from South America to Los Angeles previous to 1969 [33]. Mortality is seen in children under seven years old in the Midwest and Southeast [34]. It is said that Caucasian individuals are the most sensitive to the venom [35].

The *Loxosceles* genus in America is represented by over 90 species, which are reported as agents causing loxoscelism to *L. laeta, L. spadicea, L. rufescens* and *L. gaucho* for South America, while for the United States and northern Mexico they are *L. recluse*, *L. arizonica* and *L. deserta*. However, some authors consider that all species are capable of producing necrotic arachnidism or loxoscelism [36]. In 1997, the American Association of Poisoning Control Centers registered close to 2,000 bites by *L. recluse* (endemic in Alabama), that occurred largely during the summer months when the spiders are more active [37].

In Argentina, accidents due to *Loxosceles* rank second due to spiders and represent 4% of the total of venous animals. The majority of the arachnoids are found in home environments (57%), while the remaining 43% are located around homes [38]. In Chile, bites by poisonous animals are recognized as work accidents. Spiders are often found in warehouses, libraries, laundry mats, cleaning companies, supermarkets, clothing and hardware stores, factories, constructions sites and places adequate for their presence (food and refuge). The number of men bitten is greater than that of women [39]. In Central America and South America, *L. laeta* is endemic and known to be the most toxic, dangerous and often responsible for several deaths a year [32, 40].

In Brazil, of the 153 cases studied, 118 (71%) had skin lesions and 35 (22.9%) had visceral-skin lesions [41]. The majority of the patients were bitten in the arm or legs (29.4% in the arm and 45.7% in the leg). Since 1990, the number of people bitten by *L. intermedia* [79] increased. At pediatric hospitals in Peru, during 1964-1980, the greatest incidence occurred in babies, pre-scholars and boys, with bites seen mainly in the chest area and extremities [42, 43].

At the Mexican Institute of Social Security (IMSS), the violinist spider is not included in the list of poisonous animals that have driven almost three thousand people to the Emergency Room in the last three years, even though it is considered a dangerous arthropod [58]. *L. boneti* is a widely distributed spider in Mexico and one of the main species involved in poisoning humans [44].

Zoogeography: The *Loxosceles* genus includes at least 56 species in Eurasia, Africa and America; 54 in the American continent, one in the Mediterranean region and another in South Africa [29]. The most commonly known, *L. recluse* and *L. laeta* are located in North, Central and South America. It is possible that the extensive geographic location of certain species occurred due to their distribution in commercial articles [45-47]. In fact, they are widely distributed in regions with tropical and warm climates. The preferred climates identified are: temperate forest, rainy forest, grasslands (savanna), chaparral and desert or dunes [31]. Mascaro (1974) mentions that *L. laeta* can be found extending from the United States down to the Patagonia [48]. *L. deserta* is mainly found in the Mojave and Sonora deserts, in the San Joaquin Valley and in areas adjacent to Mexico [17, 49]. Cases of loxoscelism have been reported in Veracruz, Puebla, Morelos [7] and Mexico City [48]. Hoffman [52] and

Gerstch (1983) point to the entomogeography of the 38 species recognized in Mexico, of which 30 (78%) are endemic (Map 1) [50-52]. *L. deserta* has been reported in North and South Baja California [53]. However, until now it has not been possible to associate certain species with detected cases of necrotic arachnidism (arachnidism, araneism or arachnoidism) [54] since the majority of the times the spider remains unidentified. In Chiapas, *L. tehuana* is endemic. It is considered the most poisonous spider and the majority of the people bitten live in rural areas [55].

Similarly, *L. reclusa* is known to live on the Pacific coast of Mexico, extending from the Southern part of Sinaloa to Central America, inhabiting warm-humid and semi-dry zones [15, 56]. The *L. devia*, *L. candela*, *L. belli* species have been identified. *L. devia* is the most widely seen, followed by *L. belli* and *L. candela*. *L. belli* registers in first place in the state of Nuevo León. There is a sympathic relationship between *L. devia* and *L. candela*, in addition to *L. belli* and *L. candela* for the municipalities of Monterrey and Garcia, respectively [36].

In Brazil, *L. gaucho*, *L. laeta* and *L. intermedia* are abundant with important levels of household infestation by the latter and mortality rates of 0.2% [16, 57]. In the central zone, they are found in 41% of urban households and 24% of rural homes [58]. The age groups most affected are the first five decades. They have been found in hospital settings and academic areas [59].

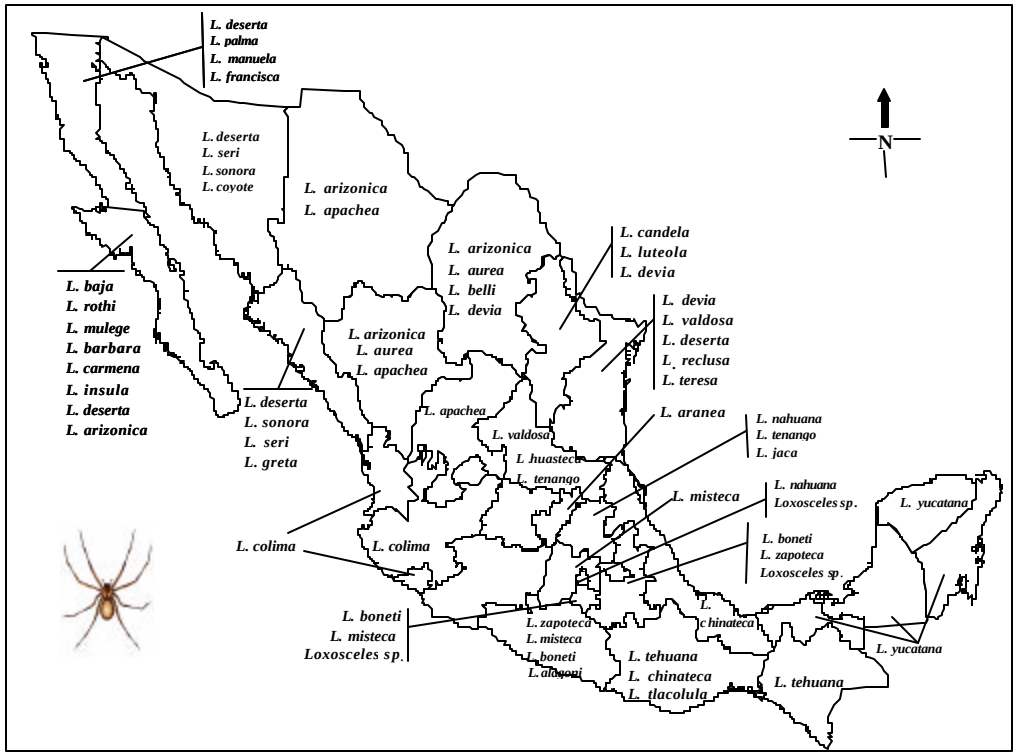
In Spain, *L. rufescens* is classified as subtroglophillic, that is to say, it lives part of the year refuged in caves and when outside, it is often found under rocks or in shady places [60].

Morphology: The *Loxosceles* genus, to which *L. reclusa* belongs ("brown recluse spider") and *L. laeta* ("South American brown spider"), are animals with bodies measuring 7-15 mm long and 0.2 to 2.5 cm in diameter dependent on diet and habitat (*L. laeta* measure 3-4.5 cm) [61, 30, 62]. *L. spiniceps* has a long body 8-10 mm and legs measuring 25-50 mm [63, 64]. They possess an external skeleton composed primarily of chitin and a body divided into two regions or tagmas [13]. The prosome is light brown or gray and the opistosome is cream olive colored (covered with fine hairs), linked by a structure called a pedicle (Fig. 1) [65].

L. arizonica varies in color from yellow to dark brown [66]. Both genera reach a weight of 0.5 g. They have six simple eyes of equal size, a diade at the front of the cephalothorax and two others towards the back and to the side of the first, forming a triangle [56, 59, 67]. Their vision is excellent [68]; however they are the only spiders that cannot see from behind since they do not have the backend eyes (Fig. 2) [69]. The legs measure 0.8-4 cm and are covered with fine hairs (with tactile function) [70] and have nails on the tarsus, longer than those of the males. The darker and more sclerosed part on the back of the cephalothorax includes a central anterior region in form of a violin, the "neck" pointing towards the abdomen [17] from where the name "violin spider" or "fiddle back spiders" derives [8, 45, 71] (Fig. 1). In the *L. devia*, there is variation in intensity and in certain species; it is difficult to identify [49]. The majority is very hairy [72].

The males differ from the females in their sac-form expansion seen in the distal segment of the pedipalpi (stridulatory apparatus) or tactile organs on the sides of the chelicerae, that correspond to the seminal receptacle or spermatic sac [58, 67]. Each pedipalple has six segments [13]. The Labidognatha suborder is characterized by its chelicerae (inoculating teeth) horizontally placed and when biting, cross over like a tweezers (Fig. 3) [70].

Biology and ethology: These spiders have night habits or are crespusculary (lucifugous), sedentary and segregary [75, 76] allowing them to catch insects and other arachnids [14, 45, 56]. Its movements are rapid in comparison to other spiders [73]. In Argentina, the following results were obtained: 0% in the morning, 14% in the afternoon and 86% are seen during the evening [38]. They live conforming dense populations (up to 2,055 collect in a single house) [77], however it has been seen that *L. laeta* and *L. intermedia* do not share the same microhabitats [34, 78]. They are often found under tree barks, in stored wood and bricks, under rocks, in livestock facilities, in bamboo plants [79], caves and museums. In houses (synanthropic environment [75], where they mainly arrive in the fall, they are often found in dark, hidden places such as bathrooms, under furniture, over blinds, attics, boxes, clothes, bed sheets, walls (preferably corners), behind frames, mirrors, dents and abandoned waste. This cryptozoic characteristic allows them to install and proliferate abundantly [80]. The majority of the attacks occur while victims are sleeping (38%) and when they are dressing (32%) [14, 18, 42, 45]. The intradomiciliary accident is more frequent at night throughout the year [72] and for *L. intermedia*, mainly during the months of October to March and between January and April in Peru [81, 82] and in the South



Map 1: *Loxosceles* species in México (Hoffmann, 1976; Gertsch, 1983 and Berea, 2003)

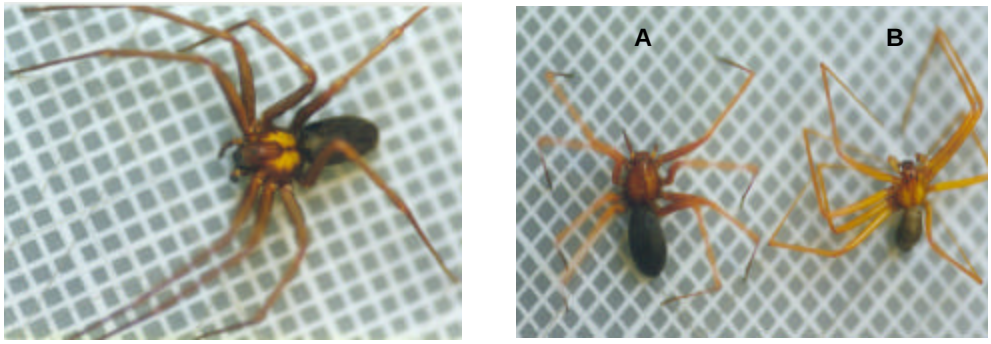


Fig. 1: Left: Female *Loxosceles sp* located in the state of Jalisco. Right: A) Female and B) Male of *Loxosceles sp*, from the state of Quintana Roo (Property of the National Collection of Acarus of the UNAM Institute of Biology, México)

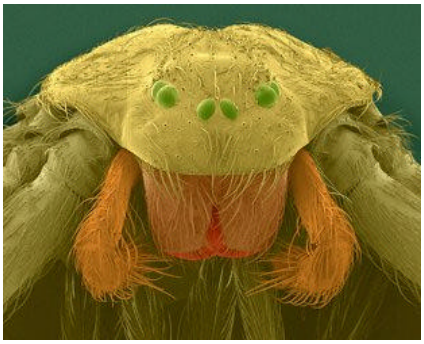


Fig. 2: Left: Electron Microscopy Microphotograph, frontal view of the cephalothorax showing the ocular formula (2, 2, 2) and the stridulatory apparatus [73, 74]

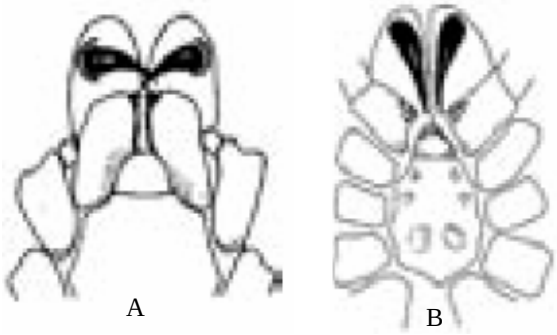


Fig. 3: Position of the inoculating hooks (arrows). A: Araneomorphae infraorder (*Phoneutria spp*), B: Mygalomorphae infraorder (Tarantula) [13]

American cone from December to May [22]. They hibernate all winter and the majority of bites occur between March and October [16, 43, 61]. The majority of the spiders rarely inflict more than a bite. Nonetheless, it is known that a woman was bitten three times by the same spider [83]. In general, females are more dangerous, particularly during mating season and during the period when they are raising their offspring (May-August) [15, 84], related to greater weight and dimensions in comparison to males, differences not found between *L. spinulosa* and *L. parrami* of medical importance in South Africa [72, 85]. In addition, as with some poisonous snakes, spiders sometimes inflict "dry" bites inoculating little or no venom, a factor that influences in the victim's response [86].

In general, mating takes place during June and July [30]. For *L. intermedia*, females have immature gonads during the months June, July and August [81]. They are more active at temperatures between 4 and 30°C, although they may tolerate freezing temperatures of over 100°F. *L. intermedia* withstand higher temperatures, while *L. laeta* tolerate lower ones [87]. They are oviparous producing up to 300 eggs during their reproductive life with an incubation period of 20-36 days [67, 84, 88]. They grow while shedding skin (exhubia), a process known as ecdisis [67]. They reach maturity at a year, after 7-12 sheds [67, 70] and a longevity of 2-4 years [7, 49, 56, 89] and more than 7 under experimental conditions and surviving 6-12 months without consuming water or food [30, 67, 90]. Life expectancy is greater in unmated animals [70].

They are basically insectivores: flies, moths, crickets, cockroaches, small arthropods and other bland body animals [17], although occasionally they feed on decomposing animals. The nymphs [91], youngsters and adults practice cannibalism [67, 70, 92]. *L. reclusa* has a predilection for dead animals [93]. In Brazil, *L. amazonica* shares a day refuge with small insects (ants and larvae), in places with little light and high humidity; *L. reclusa* prefers dry and damp places, while *L. rufescens* like fresh and humid hideouts [52, 75, 94]. Their web is irregular, lax and dirty similar to a bundle of cotton [89], without a specific pattern that serves as a refuge during the day [42, 76].

The economic importance for mankind lies on the control of many destructive insects and plagues [31]. Health benefits are the consumption of hematophagous insects that are disease transmitters [95]. Biting insects such as flies, ticks, bedbugs and killer beetles, among others, may cause wounds similar to those produced by a bite by *L. reclusa* [33].

Venom composition: Few spider venoms have been studied in detail, put it is known that they use it to immobilize being mainly cytotoxic and eat their catch [8, 12]. The *Loxosceles* venom is composed of at least 10 or 12 proteins (similar to that of the rattle snake). It is thermo-labile and its enzymatic activity is superior to that of the *Latroectus* [9, 58, 96]. It is rich in enzymes: hydrolases, lipases, peptidases, collagenases, alkaline phosphotase, 5-ribonucleotidase, phosphohydrolases, proteases, hyaluronidase, acid phosphatase and phospholipase A_2. The last three have great antigenic ability and therefore great sensitivity [97, 98]. The proteolytic effects are seen at the level of the constituents of the extracellular matrix such as fibronectin, fibrinogen, entactin and heparin-sulphate proteoglycans [99]. Some authors consider it more potent than that of the rattle snake and cobra, since amounts of 0.5 μg (no more than 30 μg of protein) cause dermal necrosis in rabbits [34, 40, 100]. In fact, the bite causes a superficial intradermal inoculation of about 0.3 ml of venom, 0.5 to 1 μl of *L. laeta* and *L. rufipes* and 0.25-0.62 μl (0.36 μl on the average) for *L. reclusa*, in general, the male produces less but the amount that the inoculum is toxic [1, 101, 102]. It has necrotizing, hemolytic, vasculytic and coagulating [58]. It produces local edema, a thickening of the endothelium, accumulation of inflammatory cells, intravascular coagulation, thrombocytopenia and hemorrhaging and necrosis. The generalized systemic symptoms such as fever, malaise, pruritus and exanthema are common, while hemolysis, intravascular coagulation, thrombocytopenia and renal failure happen in approximately 16% of the victims [103]. Nonetheless, even large amounts of the venom from *L. gaucho*, *L. laeta* and *L. intermedia* have low proteolytic, myotoxic and phospholipase A_2 activity levels [104]. After being inoculated, the venom is more rapidly disseminated lymphatically than via the blood stream [56]. It is often light colored, of viscous consistency and contains enzymes with hemolytic, gelatinolytic, fibrinonectinolytic and fibrinogenolytic activity in mammals (Table 2) [14, 57, 105]. The proteolytic action dependent on calcium on band 3 of the transmembrane protein of the erythrocytes makes them sensible to the activation of the complement with intravascular hemolysis following [106]. Hialuronidase (known as a "disseminating factor), the nucleotide similar to adenosine triphosphate and citrate are the major components of the spider venom. The hialuronidase and the citrate (anticoagulant, chelating factor and buffer) are considered active components and recently, extracellular ATP has been considered as toxic for certain cells [10, 52]. Enriched with biogenic amines,

Table 2: Elements involved in the physiopathology caused by *Loxosceles* poisoning

Venom contents	Induced by the venom
Phosphodiesterases	Histamine
5'ribonucleotide phosphohydralase	Serotonin
Sphingomyelinase B and D	Complement activation
Alkaline phosphatase	Bradikinins
Phospholipase A	Prostaglandins
Hialuronidase	Fibrinogen
Collagenase	Activation of V and X factors
Elastase	Prothrombin
L-amino acid-oxidases	Thromboxan B_2
Deoxyribonucleases	Chemotactic substances
Adenosyntriphosphatase	Interleukin 8
Acetylcholinesterase	Proteases
Metalloproteinases	Growth Factors
Polyamines (spermine)	Changes in the adhesion proteins
Gamma aminobutyric acid	Activation of polymorphonuclear cells
Histamine	Activation, expression and secretion of T cells
Serotonin	Alpha oncogen related to growth
Neurotoxic peptides	Monocytic chemotactic protein
Levarterenol bitartrate	Degradation of erythrocytic glucophorins
Antibactericide substances*	* not proven
Necrotoxin (glycosilated protein with sphingomyelinase activity	

not conceptualized within toxic fractions, they are capable of producing intense pain. Spermine may represent the final toxic product of the specialization that has occurred in certain lines of spiders during their evolution [105]. In fact, the polyaminamides, polar compounds of low molecular weight, act at the membrane stabilization level, blocking Ca^{2+} and Mg^{2+} channels, chelation of metallic ions and presynaptic and postsynaptic transmitters [107]. The acylpolyamines of low molecular weight are paralyzing and are composed of an aromatic portion containing amino acids and polyamines. These substances are main components of many poisonous spiders and are named "glutamate receptor antagonists" [10], rich in proteins with N-mannase residues (Loxolisine B) that provide the gelatinolytic activity, identified as two zymogens (serine-protease) of 85 and 95 KDa with no lamininolytic activity [99, 108]. The glycosilation of certain loxolisine B residues, a glycoprotein of 32-35 KDa, with metalloproteinase activity (endopeptidase containing an atom of zinc and secreted by connective tissue cells, phagocytes and a number of transformed cells) is important for the dermonecrotic activity. The substrates are collagen, fibronectin, elastin and alpha-1-antitripsin, among others [13, 109, 110]. The fibronectinolytic and fibrinogenolytic activities of the venom from *L. intermedia* are produced by a metalloproteinase of 20-28 Kda (Loxolisine A) [99, 110]. The bite by *L. reclusa* causes intravascular necrosis associated to spherocytosis, changes that persist for several days to a week [14, 111].

Sphingomyelinases B and D (or phospholipase D) [84, 112] are the most important skin necrotic factors. They adhere to cell membranes causing platelet aggregation, erythrolysis, damage to blood vessels, fibrinogenolysis and an Arthus type reaction [8, 71, 108, 113]. This is due to the events that involve sphingomyelinase metabolites including the inhibition of proliferation, differentiation and cell growth [40, 112] since it induces the expression of metalloproteinase 9. Similarly, the venom induces apoptosis of human keratinocytes when increasing the expression of Metalloproteinases 2 and 9. In addition, the activation of these cells causes the production of TNF-á, a cytosine involved in local inflammatory processes. The venom from *L. deserta* induces the expression of the vascular endothelial growth factor in keratinocytes, which causes angiogenesis and vascular permeability contributing to vasodilatation, edema and erythema [35, 114, 115]. Platelet aggregation is a product of the adherence of the amyloid P serum glycoprotein to the platelet membrane in the presence of calcium ions, which triggers disseminated intravascular coagulation. Sphingomyelinase catalyzes the hydrolysis of sphingomyelin and induces the intrinsic activity of lisophospholipase D towards lisophosphatidylcholine producing lisophosphatidic acid, known to be an inducer of platelet aggregation, endothelial hyperpermeability and pro-inflammatory responses [40, 112]. This enzyme has dermo-necrotic action in rabbits and is toxic in mice and horses [52]. The secretion of serotonin by activated platelets induces chemotaxis of polymorphonuclear cells towards the lesion site, contributing to local vasculitis and necrosis [13, 42]. The necrotizing activity is not associated to low molecular weight fractions such as inosine and nucleotides. Geren (1975) isolated two 34 KDa proteins that seem to be responsible for toxicity [105] and the allergenic capacity [56]. Toxin I cause characteristic lesions and is lethal for rabbits and mice. Toxin II is not toxic for mice, is lethal for rabbits but does not cause necrotic lesions [105].

Currently three isoforms (P_1, P_2 and P_3) are known with a relative mass of 28-35 KDa. P_1 hydrolyzes sphingomyelin with lesser efficiency than P_2, that may be attributed to a substitution in the 203 position (Pro-Leu) and local substitutions of amino acids in the hydrophobic channel for the recognition and linking of the substrate.

The third is inactive [76, 116, 117]. The sequence of 305 amino acids in the sphingomyelinase of *L. reclusa* is identical in 87, 85 and 60% to that of *L. arizonica*, *L. intermedia* and *L. laeta*, respectively and 84 and 46% to SMasaD 1 and 2 of *L. boneti* [112]. In addition, crossed reactivity studies suggest that sphingomyelinase D (31-35 KDa) originated in the ancestral lineage of *Loxosceles/Sicarius*. It is inferred that the bites of all of the species from this group are capable of producing dermonecrotic lesions. The response between *L. boneti* (Mexico) and *L. laeta* (South America) is attributed to the filogenetic correlation due to its geographical origin [118]. These proteins vary in molecular mass among species: 31-32 KDa for *Loxosceles* from North America, 32-33.5 for the African type and 32-33 for *Sicarius* [119].

In *L. intermedia*, the hemolytic activity dependent on the complement and the necrosis inducing factor are associated to a 35 KDa protein, known as F35 with a potent lethal effect on mice. This is generated from the third larvae stage on and increases in quantity and toxic activity as the spider reaches the adult stage which coincides with the appearance of the abilities to disseminate, hunt and defend itself deemed necessary for the survival of these spiders [16, 120]. A pronounced seasonal variation is seen in *L. laeta* in relation to the poisonous activity [121] considered more toxic than *L. reclusa* [4, 15, 52]. The venom of this species induces the production of alpha and beta kinases as the expressed and secreted regulator of the activation of normal T lymphocytes (RANTES), the monocyte chemo-attracting protein I (MCP-1), interleukin 8 (IL-8) and the alpha oncogene related to growth (GRO-a) that probably participate in the appearance of dermonecrosis mediated by neutrophils and T lymphocytes. In addition, the activation of the complement causes the release of C5b, neutrophil chemo-attractants that generate tissue damage at the site of the bite [13, 42]. Similarly, they cause the rupture of glycophorins from the erythrocytic surface, easing the activation of the complement and hemolysis [121].

In Spain, *L. rufescens* is less poisonous than *L. laeta* [120]. However, it is not a remote possibility that other species cause these types of lesions [54]. In fact, the degree of systemic poisoning varies between species [29]. The lethal dose (LD_{50}) of *L. intermedia* is 0.48 mg/kg that of *L. gaucho* 0.74 mg/kg, while for *L. laeta* is 1.45 mg/kg. The dermonecrotic and lethal activities are detected in the A fraction of the three species, whose largest protein is 35 KDa in *L. gaucho* and *L. intermedia*, but 32 KDa (reported as sphingomyelinase) in *L. laeta* responsible for necrotic damage. All contain common residues in their N-terminal sequences. The identity is 50% between *L. gaucho* and *L. reclusa* and 61.1% between *L. intermedia* and *L. reclusa* [10, 104]. Ontogenic differences are seen in the venom action in *L. intermedia*, being more lethal and dermonecrotic that of adult spiders than those from newborn and of greater potency in females [13]. The volume that they inject when biting is in direct relation to the time that has passed since they last ate, with greater availability of venom if submitted to prolonged fasting [121].

On the average, they produce 0.1 mg of venom (0.15-0.45 µl) by electrical stimulation with 1.5 volts on the cephalothorax [13, 42, 76], place where the poisoning apparatus is located, composed of continuous apocrine glands, covered by secretory epithelium and surrounded by muscle cells. From *L. laeta* we can obtain 60 µg, while from *L. intermedia* and *L. gaucho* 30-40 µg [106]. From dissected glands, 0.8 µg of toxin can be obtained [120, 121].

In conclusion, this paper provides general information related to the "violin" spider, *Loxosceles sp*, its distribution in México and other countries, thus as the venom composition and its effects and cosequences in humans and animals.

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