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Venomous and poisonous arthropods in Iran, West Asia, and the Middle East: an overview of their identification, bites, stings, behavior, biology and geographical distribution

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ABSTRACT

Arthropods belong to the invertebrate Phylum Arthropoda, which contains the most species on Earth. Venomous arthropods are among the most important animals that live in abundance in the human environment. The current study gives an overview of the importance of their identification, bites, stings, behavior, biology, and distribution in the geographical region of Iran, West Asia and the Middle East. The databases have been searched comprehensively and the most relevant Published articles and books from 1978 to 2023 were carefully selected based on the most appropriate keywords. Biting and stinging venomous creatures of arthropods, class, order, and family were presented in the tables and their importance and role of each order in the bite, sting and the occurrence of hazards were determined separately. Finally, the methods of preventing their bites and stings were recommended. The phylum of arthropods in Iran has two subphylums including Chelicerata with one Class, five Orders, and 25 families, and Mandibulata with three Classes, nine Orders, and 29 families. They are scattered all over Iran. Their venom apparatus includes venom gland, modified pedipalps, chelicers, stinger in the tail (telson), mouthparts such as hypostome, fangs or forcipules, appendages (mandibles), proboscis, ovipositor (stinger), and hair (urticating bristles). The importance of venomous animal stings and bites in the training programs of physicians, the medical and nursing staff is very weak or does not exist at all. To achieve and enhance the management efficacy of bites and envenomation, more accurate information about venomous creatures and their venom composition is required.

Keywords

Venomous arthropods, poisonous, Insect, Bites and stings, Iran, Middle East

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Introduction

Venomous animals have undergone evolutionary adaptations, leading to the development of venoms with a distinctive chemical composition that can interfere with the physiological systems of vertebrates. Consequently, this interference can result in biological malfunction or even death. Throughout evolution, numerous animal groups have independently evolved venom-producing organs and specialized injection apparatuses. Over the course of this extensive process, venoms have acquired unique properties and high potency, enabling them to effectively target their molecular counterparts [1]. Approximately 15% of the estimated 1.7 million animal species are venomous, with a significant portion of these creatures belonging to the phylum Arthropoda [2].

Arthropods employ their venom for various purposes, including immobilizing and capturing prey, deterring predators, and facilitating food digestion. Additionally, some arthropods utilize their venom for intraspecific competition. Despite humans harboring a deep-seated fear of venomous animals, there has always been a fascination with them [3]. This fear can be attributed to historical myths, narratives, and the negative portrayal of these creatures in the media. It is important, however, to acknowledge that certain venomous animals, such as snakes, are responsible for tens of thousands of reported deaths and injuries worldwide. The World Health Organization (WHO) has even reclassified snake envenomation as a neglected tropical disease. Paradoxically, over the past few decades, there has been an increase in global popularity and interest in keeping poisonous snakes, spiders, scorpions, and centipedes as pets in captivity.

Recent scientific research has been focused on exploring the potential benefits of animal venoms and toxins in various applications. These include their use as molecular research tools to study physiological processes, as templates for developing novel drugs with diagnostic and therapeutic purposes, and even as agents for pesticides and anti-parasitic treatments [4-8]. Researchers have been actively involved in continuous studies aimed at producing effective and safe drugs, and they have made promising discoveries regarding the beneficial effects of animal toxins. Despite their toxicity, venoms contain components that exhibit a wide range of therapeutic potential. These scientific advancements have altered the perception of venoms from being solely deadly substances to having therapeutic value. Currently, numerous studies are underway to identify their molecular targets, such as ion channels and receptors, as well as to explore their pharmacological properties for the development of new drugs [9-11]. More than one million species of arthropods have been identified. These invertebrates, belonging to one of the most successful and prevalent phyla in the animal kingdom, inhabit various environments including land, air, and water [12-17]. Venom has evolved in different groups of arthropods, enabling them to adapt to their respective habitats. Over millions of years of evolution, arthropods have developed sophisticated mechanisms for delivering their venoms to prey, effectively fulfilling their defensive and predatory goals. The morphological diversity of arthropods' venom apparatuses is astonishing, encompassing various structures such as modified pedipalps, tails (telson), mouthparts like hypostomes, chelicerae, proboscises, ovipositors (stingers), and specialized hairs (urticating bristles) [18-22].

Nowadays, with the advancement of technological capabilities, new avenues have emerged for understanding the properties of venom. Venom is a significant natural biological resource, harboring potent compounds that hold great promise in targeted therapies. Each venom contains multiple components with potential therapeutic value, offering a diverse range of applications in the development of life-saving drugs, research tools, and also, environmentally friendly insecticides. The majority of published articles focus on medically important arthropods, exploring their venoms, compositions, biological activities, and the medical implications of envenomation or stings on humans. However, there has been relatively less emphasis on other vertebrate groups. In light of this, this review aims to encompass all venomous and poisonous arthropods, including biting and stinging families, while placing particular attention on their distribution in West Asia and the Middle East, with Iran as a focal point (Figure 1).

Figure 1.
Map of Middle East and West Asia (Prepared by Dehghani R)

Arthropods, like other wildlife, transcend political borders and are found in habitats worldwide based on their natural requirements. They exhibit remarkable adaptations and thrive in diverse environments. Consequently, studying these creatures in Iran extends beyond its geographical boundaries, encompassing neighboring countries that share common features despite having distinct climates.

Data collection: Sources and Methods

The study was conducted using the review method. Based on highly relevant keywords such as arthropod, venomous, poisonous, biting, sting, class, order, family, terrestrial, and aquatic, extensive searches were performed in electronic databases including PubMed, EMBASE, Google Scholar, Scopus, Web of Science, and CINAHL covering the period from 1978 to 2023. The most appropriate articles and books that satisfied the criteria regarding arthropod species in the Middle East and Iran were selected. A total of 324 carefully chosen articles and books were derived from approximately 500 sources. In the tables 1 and 2, biting and venomous animals belonging to the phylum Arthropoda, as well as their respective subphyla, classes, orders, and families, are presented along with information about their venom apparatus or sting structure. Additionally, their significance in terms of biting and stinging incidents and their contribution to injuries were separately determined. Finally, recommendations for methods to prevent and treatment their envenoming were provided.

Findings

The importance of biting, stinging, venomous, and poisonous arthropods

Among the animals, there is no group that has as many chemical defense mechanisms as arthropods. The study of arthropods' defense mechanisms, particularly against predators, has been extensively researched. Arthropods are classified into two categories based on their defense mechanisms: venomous, which actively inject their toxins using specialized structures, (like stingers), and poisonous, which passively release their toxins when handled, pressed, crushed or consumed [23-25].

There are two major types of defensive substances in arthropods; those produced by specific exocrine glands and substances that have essentially no glandular origin. These substances can be found in the blood, stomach, or other parts of the body, either internally or on the body's surface. Glandular secretions can be classified into two groups: the first group consists of injectable substances delivered through a stinger in scorpions, bees, and chelicerae in spiders. The second group contains non-injectable substances, such as rove beetles, blister beetles, and millipedes, which lack injecting organs [26-28]. Arthropods are distributed worldwide, but their species distribution and diversity are particularly high in tropical and subtropical regions [29].

Iran with an area of 1648,000 square kilometers is located in West Asia and the Middle East and has a tropical and subtropical climate that supports high diversity of arthropods. Venomous and poisonous arthropods of Iran, are in two sub-phylums; Chelicerata and Mandibulata. It is worth mentioning that this distribution is not exclusive to geography of Iran; other countries in the region also host similar arthropod species, although the proportions may vary (Figure 1, Table 1).

Subphylum Chelicerata

Chelicerata is the second largest group of arthropods with one class, Arachnida (Table 1). The subphylum Chelicerata has a pair of highly specialized organs, called chelicers instead of mandibles which is modified and seen as scissors or pincer-like. Many species in this group are venomous and are medically important in health and medicine.

Arachnida class

The class Arachnida includes the most important venomous members, such as scorpions, spiders, and ticks (Figure 2). Certain orders within this class, such as Solpugidae are predators, with the segmented abdomen and highly bigger chelicers than spiders. Unlike spiders, they do not possess venom, but because of their aggressive behavior, they cause fear and panic. Sulpogida bite in self-defense, which can cause tissue wounds, contamination of these wounds with soil microbial agents may cause severe infection.

Scorpiones order

Up to now, 2231 scorpion’s species in 208 genera and 20 families have been documented worldwide [30,31]. Approximately 50 species are medically important, most of which are found in the Buthidae family. The most dangerous scorpion’s species have been reported across regions including Africa, Middle East, South America, Central, and North America, and Asia [32,33]. Among arthropods, Scorpion stings and injuries are most frequently observed in Iran. The occurrence of scorpion sting accidents and the extent of damage in different parts of Iran depend on several factors such as the local way of life, socio-economic status, housing conditions, availability of healthcare facilities, and the specific scorpion species present in each geographical region. In Iran, 68 species, 19 genera belonging to 4 families have been

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Table 1.
Venomous and poisonous arthropods present in Iran (prepared by Dehghani R)

Subphylum	Class	Order	family	common name	Venom delivery apparatus
Chelicerata	Arachnida	Scorpiones	Scorpionidae	scorpion	Stinger
			Hemiscorpidae		
			Buthidae		
			Diplocenteridae		
		Aranida	Theridiidae	Chelicerae	Chelicerae
			Sicariidae	Brown widow	
		Acari	Ixodidae	Hard tick	Hypostome
			Argasidae	Soft tick	
		Pseudoscorpiones	12 families	False scorpion	Pedipalps
		Solifugae	Galeodidae	Solifuge	Not venomous, but bite with Chelicers
			Karschiidae		
			Daesiidae		
			Glyppidae		
			Rhagodidae		
Mandibulata	Diplopodia	Spirostreptida	Cambalidae	Millipede	Dermal glands
	Chilopoda	Sclopendromorpha	Sclopendridae	Centipede	Forcipules
		Lithobiomorpha	Lithobiidae		

reported. The stings of Androctonus crassicauda (Olivier, 1807) and Hemiscorpius leptorus (Peters, 1861) species are particularly dangerous, with documented cases of mortality associated with their stings, especially in the southern region of Iran [34-37]. The venom of Androctonus species is neurotoxic, while that of Hemiscorpius species is cytotoxic. The sting of scorpions with neurotoxic venom causes severe pain and neuromuscular blocking activities by inhibition of nerve-mediated twitches while the sting of scorpions with cytotoxic venom led to local necrosis, including myotoxicity, kidney degenerative glomeruli and necrotic tubular, heart myocytolysis and intestinal edema of lamina propria, and villous necrosis [38,39,40,41,42]. Scorpions are distributed in a wide range of habitats, both inside and outside houses as well as in the fringes of villages or cities. They are particularly abundant in the eastern and western regions of Iran and their stings can be quite painful.

Currently, the primary method of treating scorpion stings in Iran involves the use of antivenom serum that is produced domestically [43-45]. To minimize the occurrence of scorpion stings in any region of Iran, it is essential to improve residential housing conditions and prevent the entry of these creatures into suburban areas. Also, capturing or repelling these animals can help to avoid or reduce the risk of being bitten by them [46,47].

Araneida order

Spiders are predatory arthropods that play a crucial role in controlling pests' populations and maintaining ecosystem balance. Nearly 40,000 species of spiders have been described worldwide, from which approximately 200 species posing a threat to humans. Spiders have a global distribution and some of them are able to survive even in urban environments, occasionally coming into contact with humans under certain conditions. However, spiders tend to living in the desert [48,49]. Most spiders are not considered harmful to humans due to their harmless venom or the small amount of injectable venom, their small chelicerae size, their lifestyle, and their non-invasive behavior [50]. Spider venoms can be classified into two main groups; neurotoxin and necrotoxin, based on their mechanism of action. Black widow spiders possess highly potent neurotoxic venom that affects the nervous system of insects and mammals. The second

class	Order	Family	Figure	References
Arachnida	Scorpionda	4 families		Prepared by Dehghani R
	Aranida	Theridiidae		Prepared by Dehghani R
		Sicariidae		Zamani et al., (2014) with permission
	Acarina	Ixodidae		Prepared by Dehghani R
		Argasidae		Prepared by Dehghani R

Arachnida	Pseduscorpionda	12 families		Cokendolpher et al., (2019) with permission
	Solifugae	5 families		Prepared by Dehghani R

Figure 2.
Stinging, biting, and venomous agents belong to orders of the Arachnida class. (Prepared by Dehghani R)

group includes brown widow spiders, whose venom is necrotic and causes skin lesions. This venom causes tissue injuries and cell apoptosis, and various symptoms such as nausea, vomiting, chills, fever, muscle pain, general purpura rash, hemolytic anemia, acute renal failure, shock, coma, and even death [51-53

In Iran, the species of Latrodectus from the Theridiidae family, commonly known as black widow spiders, have been frequently reported. Many of these spiders are medically important as they are capable of envenoming in humans. Latrodectus species can be found in most parts of the world, except for cold regions in Europe and Asia. Almost all species within this genus are highly important in medical and veterinary sciences. So far, about 30 species in the genus Latrodectus have been identified in the world from this, five species have been reported in Iran [54,55].

Black widow spider bites cause a range of clinical symptoms which is known as Latrodectism. The major component of its venom is α-Latrotoxin (α-LTX) [56]. The toxin is characterized by its ability to rapidly release acetylcholine from nerve terminals and endocrine cells in vertebrates. As a result, toxin causes systemic clinical complications in the victims and in severe cases disturbs the cardiovascular system, respiratory system, nervous system (including the peripheral and autonomic branches), skeletal and smooth muscles, gastrointestinal tract, urinary system as well as causing localized skin reactions or marks [57-61].

Brown widow spiders, specifically those belonging to the Loxosceles genus, are commonly referred to as recluse, violin, or fiddle-back spiders and belong to the Sicariidae family. All these species possess venom with necrotic properties, making their bites dangerous. Among the 117 species worldwide, only Loxosceles rufescens (Dufour 1820) has been identified in Iran. This species was initially reported in Tehran province and subsequently in Hormozgan and Fars provinces [62,63,64]. Brown spiders, known for their shy nature, typically inhabit quiet, dark, and isolated places. They do not exhibit aggressive behavior but may bite if provoked, trapped against the skin, or accidentally touched. However, multiple bites from these spiders are uncommon. Anti-venoms are available for Loxosceles spp. envenomation. The severity of reactions to their bites can vary depending on factors such as the amount of venom injected, the bite location, the age of the victim, and their overall health conditions.

Treatment for Loxosceles spp spider bites typically involves the administration of steroids, antibiotics, hyperbaric oxygen therapy, wound debridement, and scar repair. However, the effectiveness of treatment can vary from person to person [56, 61, 65]. Given the widespread distribution of medically significant spiders in Iran, accurate diagnosis is crucial for appropriate treatment and preventive measures. Incidences of bites by venomous animals like widow spiders tend to be more common in areas surrounded by natural open spaces, such as the suburbs of cities and villages.

In the summer of 2017, in the city of Kashan in central Iran, a 48-year-old female cleaner was bitten by a spider while collecting garbage. The spider was later identified as a member of the Loxosceles sp (Araneae-Sicariidae). The initial symptoms she experienced included immediate irritation, itching, swelling, redness on her arm and numbness in three of her fingers. She also suffered from shortness of breath. After four days, her hand became edematous and painful, and she also experienced insomnia. Her condition worsened to the point where she lost the ability to move her fingers. Due to the severity of her condition, she was hospitalized for four days and received various treatments including normal saline, corticosteroids (dexamethasone), antibiotics, antihistamines, and analgesics. Additionally, she was administered a tetanus vaccine and tetabulin [60].

Acarina Order

Ticks are classified into two families: Ixodidae and Argasidae. The Ixodidae family consists of hard ticks, whereas the Argasidae family includes soft ticks. In Iran, there have been reports of 26 species of ticks belonging to both the Argasidae and Ixodidae families, which are distributed throughout the country. Ticks are considered dangerous obligate hematophagous (blood-feeding) arthropods and are the most important vectors of pathogens. While blood-feeding on a host's, they firmly attach themselves by producing cement that secures their hypostome in the host's skin [66-71]. Their salivary secretions are highly toxic, particularly in hard ticks. Depending on the species, tick saliva contains a complex mixture of various pharmacologically active compounds that play a role in regulating the secretion of salivary proteins and countering host defense mechanisms. The composition of tick saliva changes as the feeding process progresses and the tick encounters the dynamic host response. Furthermore, the precise composition may vary among different tick species. The common constituents found in tick saliva include anticoagulants, anesthetics, immunosuppressants, vasodilators, thrombin inhibitors, proteases and protease inhibitors, anti-inflammatory compounds, inhibitors of platelet aggregation, metalloproteases, and phospholipase A2. The specific antihemostatic agents differ among tick species and genera; however, they have not been thoroughly investigated or explored [70-72].

Moreover, ticks are capable of producing a variety of other molecules with diverse biological activities. These include components found in the cement cone, cardiotoxic factors, neurotoxins, various enzymes, and enzyme inhibitors. As a result, tick saliva can be harmful as it serves as a vehicle for transmitting a wide range of tick-borne pathogens into the host's bloodstream. These pathogens encompass viruses, bacteria, rickettsia, and protozoa, which have the potential to cause diseases such as Lyme disease, babesiosis, tick-borne encephalitis, Crimean-Congo Hemorrhagic Fever (CCHF), Tularemia, and Q fever in both humans and animals [71-75]. Due to their ability to infest multiple hosts, ticks can transmit a wide variety of diseases, posing significant challenges in the fields of medicine and veterinary medicine. Ticks secrete their salivary paralyzing neurotoxin into the hosts through their hypostome, numb the bite site, and can cause an acute, progressive, symmetrical, muscle paralysis, which can potentially be fatal. Early detection and prompt removal of ticks are crucial for facilitating faster recovery from tick paralysis. Although ticks can attach and enter their hypostome anywhere on the body, they tend to attach to the scalp due to its warmth, hair density, and suitability for hiding [73-75].

The presence of anticoagulants and other components in tick salivary secretions can cause redness, local skin hematoma, swelling and rashes, which are the most common signs of tick blood-feeding on humans. The symptoms may resemble the bites of other venomous animals, and can potentially result in secondary infections caused by opportunistic microorganisms. Therefore, it is important to learn about tick bites and prevention methods. It is necessary to adhere to health standard guidelines in animal shelters and residential areas for both humans and animals [69,76,77].

In 2006, a 48-year-old woman with head and neck edema, fever and imbalance visited a clinic in Tehran. She had traveled to the mountainous regions in early spring. During the physical examination, a small tick was found firmly attached to the head, which sent to the Razi Vaccine and Serum Research Institute after being removed. This tick was identified as the female Dermacentor marginatus (Sulzer 1776) (Acari: Ixodidae). After removing the tick, the patient recovered [78].

In 2019, a 71-year-old woman from northern Isfahan Province, referred to local health center because of a burning sensation, pain and a red bumps and hematoma on her neck without fever. The clinical examination detected an arthropod attached to the neck, which was identified as a female Hyalomma spp (Acari: Ixodidae) tick. Tick was completely engorged and measured 20 mm in length. The patient was discharged after prescription of cephalexin 500 mg every 6 hours and Ibuprofen 400 mg/orally every 8 hours. The patient underwent monitoring for the next 10 days for any symptoms of tick-born disease such as Crimean-Congo hemorrhagic fever [79].

Table 2.
Venomous arthropods present in Iran (Prepared by Dehghani R).

Subphylum	Class	Order	Family	common name	Venom delivery apparatus
	Hexapoda	Hymenoptera	Vespidae	Wasp	Stinger (modified ovipositor)
			Formicidae	Fireant	
			Mutilidae	Velvet ant	
			Apidae	Bee	
		Hemiptera	Corixidae	Water boatman	Bite by proboscis or rostrum or piercing cylindrical beak mouthpart, needle-like
			Belostomatidae	Giant water bug	
			Notonectidae	Back swimmer	
			Nepidae	Water scorpion	
			Reduviidae	Assassin bug	
			Anthocoridae	Minute pirate bug	
			Nabidae	Damsel bug	
			Coreidae	Coreid bug	
			Pentatomidae	Stink bug	Thoracic glands
		Coleoptera	Staphylinidae	Rove beetle	Haemolymph
			Meloidae	Blister beetle	The release of Coelomic fluid or Haemolymph
			Dermestidae	Skin beetle	Urticating bristles on larvae
			Oedemeridae	False blister beetle	Corporal fluid
		Lepidoptera	Saturniidae	Giant silkworm moth	Urticating bristles on larvae
			Thaumetopoeidae	Oak processinary moth	
			Lymantriidae	Tussock moth	
			Lasiocampidae	Snout moth	
		Diptera	Asilidae	Robber fly	Mandibles and Hypopharynx
			Sciomyzidae	Marsh fly	
			Tabanidae	Hourse fly	
			Cecidomyiidae	Gall midge	
		Neuroptera	Myrmeleontidae	Antlion	Maxillae/mandibles

Also, in 1999, tick paralysis was reported among 400 nomadic sheep flocks in Iran. Thirty of them were affected over three days of which 15 ewes died. They showed ascending posterior paralysis, sternal recumbency, an inability to raise the head from the ground, no response to pricking the skin with a needle, and finally, lateral recumbency, deep coma, and fully dilated pupils before death. Less than 15 female ticks of Ornithodoros lahorensis (Neumann 1908) (Acari: Argasidae) were found in the carcass of dead and sick animals. The affected ewes were treated subcutaneously with 0.2 mg/kg ivermectin. All affected ewes had fully recovered after 12 to 24 hours [80].

Pseudoscorpiones order

Until now, toxic components have been identified in three of the four venomous arachnid orders, which include scorpions, spiders, and ticks. However, no information is currently available on the venom and venom glands of the fourth group, pseudoscorpiones [81]. Pseudoscorpiones are very small arthropods, ranging from 0.5 to 5 mm in size. They are commonly known as false scorpions or book scorpions, lacking a tail or stinger on their posterior end. Pseudoscorpiones have a widespread distribution all over the world, inhabiting various terrestrial habitats such as soil, leaf litter, caves, and coastal areas. They possess a unique venom delivery system in the chelal fingers of their pedipalps, which has evolved independently from that of scorpions and spiders. Additionally, some pseudoscorpiones possess another form of venom delivery called "lamina defensor," where the venom glands arise at the base of the venom tooth. They possess a pair of fingers called pedipalps, as well as one or two venomous glands that they use to immobilize their prey. However, in some pseudoscorpiones families, these venom glands are absent [82].

In 2006, Santos and colleagues [83] conducted research on the effect of Paratemnoides elongates (Banks 1895) venom, extracted from chelal hands on the rat cerebral cortex. The results indicated the possible antagonistic action of specific compounds in its venom to inhibit the binding of the excitatory neurotransmitter L-glutamate (L-Glu) to its specific sites and also decreases the GABA uptake. Additionally, in 2019, Krämer et al., successfully extracted pure venom compounds from pseudoscorpiones Chelifer cancroides (Linnaeus 1758) [84]. Studies have shown pseudoscorpion venoms contain peptides with antimicrobial properties [84]. Species of the pseudoscorpions order in Iran have received less attention due to their small size, hidden habits and habitats, and lack of significant economic importance. In 1918, the European scientist Redikorzev was the first who described and recorded them from Iran. He also described the new species, Chelifer Spinipalpis (Redikorzev 1918) [85]. Up to now, 68 species of this order in 12 families have been identified in various regions of Iran. However, there is no documented reports regarding their medical importance or their bite in Iran [86-89].

Solifugae order

Solifugae include 1000 known species) [90]. They are among the arthropods that play a crucial role in maintaining the ecological balance. Their anatomy consists of two primary divisions: the abdomen and the cephalothorax. Solifugae possess chelicerae that vary in strength across different species, facilitating the tearing of their prey) [91]. They can grow up to 12 to 15 cm in size, and have noticeably large pedipalps, which often are larger than their front legs. Although Solifugae tend to be more active at night, some species are active during the day) [92.93]. Their pedipalps have a variety of hairs and papillae that are various in different families, they play a key role as mechanical and chemical receptors [94,95]. Unlike spiders, they are not venomous. Only one case has been reported of a venomous Solifugae species from India, which caused the death of mice with its venom. However, it should be noted that no other reports have confirmed this claim.

In general, Solifugae species are not dangerous, and only in rare cases, such as when threatened by humans, they may become aggressive, make noise, and bite in self-defense. Due to their strong chelicerae, they can cause deep puncture wounds that may lead to contaminated wounds. Solifugae species primarily inhabit hot, dry, semi-arid, or desert areas. They tend to be more active in regions with spring and summer temperate climates [96-103].

A number of studies have confirmed the existence of several species of these animals in Iran [104-107]. However, they have been less studied in neighboring countries [99,108-111]. Gaining sufficient knowledge about the biology and behavior of these animals and seeking advice from experts can greatly reduce feeling of insecurity and unfounded fear (Figure 2).

Subphylum Mandibulata

Mandibulata is the largest and most divers subphylum of arthropods, comprises of three classes including Diplopoda (Millipedes or Millipede)., Chilopeda (Centipedes or Centipoda), (Table 1) and Hexapoda (insects), (Table 2) with a total of 14 orders, and 54 families. Mandibles are a unifying feature of the Mandibulata. Many species, within this subphylum are venomous and hold significant medical importance in the field of health and medicine (Table 1).

Diplopoda class

Diplo mean twofold and pods mean foot, a class of arthropods, commonly called Millipedes. Millipedes live in damp, dark places such as under rocks, or in rotten woods. They avoid light. They feed on decaying plants and other vegetation on the ground, and sometimes they also consume animal-based materials like earthworms, snails, and insects [112]. (The class Diplopoda consists of 16 orders and 140 families that are distributed worldwide. They are generally considered harmless. However, certain tropical species may pose a threat to humans when defending, [113-115]. Their medical importance arises from their ability to release an irritating defensive liquid through pores located along their sides. The defense mechanisms of millipedes can potentially harm humans, in some cases and resulting in erythematous, purpuric, and cyanotic lesions accompanied by local pain and paresthesia. Their toxin contains compounds such as benzoquinones, aldehydes, hydrocyanic acid, and various other substances [116].

Spirostreptida order

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The Spirostreptida order has been reported in Iran. These diplopods do not have stings, but they possess secretory glands located in each of their body segments. From these glands, a toxic liquid may leak out, leading to the development of erythema and brown or black spots on the affected skin. It may take several months for these markings to disappear. The majority of injuries occur when individuals wear shoes without inspecting the insides, as millipedes often seek dark and quiet locations to take refuge and rest [117]. In response to enemies or threat stimuli, some species curling into a spiral shape, and their defensive apparatus releases irritant liquid toxic that damage human skin. This toxic contains hydrogen cyanide, benzoquinones, esters, phenols, and aldehydes which cause irritation, pain, and blisters at the site of skin contact and also pain and irritation in the eyes [118,119]. Millipedes cause acute inflammatory lesions without major effects. Immediate use of alcohol or ether on the site of contact is recommended, because they can dissolve toxins. As first aid, the eyes should be irrigated with water and the patient should be referred to an ophthalmologist. In severe cases injuries can lead to blindness [120,121].

Chilopoda class

Chilo means jaw and pods means foot. Centipedes or Chilopoda are dorsoventrally flattened with numerous segments, each having one pair of legs. They possess a pair of venomous front legs on the cranial segment that is modified into special apparatus equipped with toxin hooks, used for injecting venom into prey. They have a pair of long, jointed antennae consisting of 12 or more small segments on their heads. These animals have simple eyes. Centipedes mostly live in tropical countries, active and hunting at night and feeding on a variety of insects and other arthropods. The large species may also hunt mice. Some centipedes live in buildings and move quickly. About 1700 species of centipedes have been identified. Scolopendra gigantea (Linnaeus 1758) is up to 100 mm long and has 21 pairs of legs. The centipedes found in Iran and neighboring countries consist of 48 species, of which 17 species have been reported exclusively from Iran so far [122,123].

Sclopendromorpha and Lithobiomorpha orders

The species of these orders have been reported in Iran. They are the only species in which the bite by some of them in humans can lead to death. Scutigera (Cermatia) sp (Wood 1867) is one such species. It can grow up to 25 mm in length, and has 15 pairs of legs, long and narrow antennae and compound eyes. These creatures typically reside in buildings, move quickly, and feed on insects. The bite of Scolopendra valid (Lucas, 1840) species has been reported from Ahvaz, a city located in the southwest of Iran and the capital of Khuzestan province. It bites cause various clinical and laboratory manifestations including pain, skin inflammation, itching, hematuria, and hemoglobinuria. Some researchers have suggested that these species may contain substances such as 5-hydroxytryptamine, hemolytic phospholipase A2, and a cardiotoxic protein [123,124,125]. The venom proteins of these species are highly diverse, and the majority of them are dissimilar to proteins and peptides found in venoms of other animals. This underscores the distinctiveness of centipede venoms (Figure 3) [126,127,128].

Hexapoda (Insecta) class

The class Insecta is adapted to various environmental conditions, primarily inhabiting land, although some species can be found in both aquatic ecosystems and terrestrial habitats. Their head is composed of six fused segments, and their thorax consists of three fused segments with three pairs of jointed legs and two pairs of wings. Their abdomen consists of 11 or fewer segments and lacks appendages for movement. Insects possess compound and simple eyes. With more than 800,000 species, there are six orders of insects classified as venomous and biting species (Table 2).

Hymenoptera order

The order of Hymenoptera consists of four families: Apidae (bees), Vespidae (wasps and hornets), Mutillidae (velvet ants), and Formicidae (all ants, specifically, fire ants). These families are the most clinically important in this order and their sting have been reported in Iran. They produce venom, which they use it for defending their territory against predators, obtaining food, and ensuring survival. In general, members of these families are capable of stinging multiple times, with the exception of bees [129,130,131]. While most stings only cause minor issues, it's important to note that the majority of deaths resulting from Hymenoptera stings are due to immediate allergic reactions and anaphylaxis. The venom of Hymenoptera is a complex mixture of biologically active molecules, such as enzymes, amines, glycoproteins, and peptides. A variety of these compounds are allergens that can induce allergic reactions in victim's body [131,132].

In non-allergic individuals, massive envenomation and other complications can potentially result in death. For most mammals, the estimated lethal dose is approximately 20 stings per kilogram of body weight. However, it's important to note that the dose or number of Hymenoptera stings does not influence or prevent anaphylactic reactions since these reactions are

class	Order	Family	Figure	References
Diplopda	Spirostreptida	Cambalidae		Prepared by Dehghani R
Chilopoda	Sclopendromorpha	Sclopendridae		Prepared by Dehghani R

Figure3.
Biting and venomous agents belong to Diplopoda and Chilopoda classes (Prepared by Dehghani R)

not dose-dependent. After insect stings, four possible reactions have been observed including the local reactions, regional reactions, systemic anaphylactic reactions, and less frequently seen delayed-type hypersensitivity. The onset of life-threatening anaphylactic symptoms usually appears within 10 minutes after the sting. Prompt diagnosis and initiation of treatment are crucial for successfully managing anaphylactic reactions caused by Hymenoptera stings [133-135].

Insect stings, particularly from bees, can result in various complications such as pancreatitis, hemolysis, rhabdomyolysis, nephritis, and acute renal failure The death of the victim may be attributed to kidney failure or cardiac problems [136-143. In most cases, pain and discomfort resulting from hymenopteran stings resolve within a few hours even without [144-147

In the summer of 2020, a 3-year-old boy was attacked by a group of hornets (Hymenoptera -Vespidae). The insects stung him on his head, arms, back, and buttocks. Upon arrival at the hospital, he was conscious but lethargic, and approximately 30 painful sting sites in the form of hyperpigmented papular lesions (papular urticaria) were observed on his body. Although his head and neck did not show signs of redness (erythema), his limbs, neck, face, lips, and eyelids became increasingly swollen. Additionally, his urine output decreased (oliguria), and the urine test revealed proteinuria and hematuria. The patient initially experienced stress-induced hyperglycemia, and he was unable to open his eyes. His clinical condition progressed to multiple complications, including gross hematuria, intravascular hemolysis, and myoglobinuria, anemia, thrombocytopenia, rhabdomyolysis, acute renal failure, hepatocellular necrosis, epistaxis, and respiratory distress. Metabolic acidosis and respiratory alkalosis were confirmed through a blood gas test. An abdominal ultrasound examination detected a notable bloody fluid in both sides of the subphrenic region, Morrison and splenorenal spaces, as well as the pelvis. Despite supportive treatments, his condition worsened, he was admitted to the ICU due to critical illness. He received various interventions, including administration of normal saline, a diuretic agent (furosemide), insulin, corticosteroids (dexamethasone), dopamine, and a calcium supplement. In addition, sodium bicarbonate was administered to address urine alkalinization, and blood transfusion and plasmapheresis were performed twice. Intermittent hemodialysis was also performed five times to manage acute tubular necrosis (ATN) caused by hemolysis and rhabdomyolysis. The lesions were treated by applying topical corticosteroid, zinc oxide, and Aloe Vera gel. After two weeks of hospitalization, the papules at the sting sites became necrotic. The liver enzymes reached normal levels, urine output increased, and the functions of other organs returned to normal. After 19 days of hospitalization, the patient was discharged in relatively good general condition [148].

Apidae family

Bees normally live socially and become aggressive, attacking, and stinging in groups if threatened or if their nest is disturbed. Humans may be stung repeatedly by a large number of bees simultaneously, which worsens the problem [149-153]. Honey bees can only sting once because they have barbs (hooks) on their stingers that cannot be pulled out from skin. Consequently, they lose their stinger after stinging and die due to the detachment of the apparatus from their abdomen.

Clinical symptoms of bee sting include erythema, swelling, and pain at the site of the sting. Apamin, is the main neurotoxin peptide found in honey bee venom. It has the ability to directly affect the central nervous system (CNS) by crossing the blood-brain barrier (BBB), increasing neuronal excitability, and potentially triggering seizures. Additionally, when experimentally injected into rats, it can affect K+ channels in cell membranes, leading to convulsions [23,154]. The second major component of bee venom is melittin, which is responsible for the hemolysis of red blood cells and the sensation of pain.

Vespidae family

Wasps defend their colony when disturbed or threated. They use their stings to temporarily paralyze prey for egg laying or kill it for food. Unlike honey bees, wasps are able to sting multiple times. The venom of wasps and bees is complex mixture of hyaluronidase, phosphatase acid and lysophospholipase, histamine, dopamine, norepinephrine, serotonin, and mast-cell degranulation protein. Two species of the Vespa genus from the Vespidae family have been reported in Iran, namely Vespa carbro (Linnaeus 1758) and Vespa Orientalis (Linnaeus, 1761) which are widely distributed [130,132,152,155].

Mutillidae family

Members or velvet ants are not invasive, they are usually stinging individually for defense. These arthropods are known as "cow killer ants" by the reputation of female sting that is so potent and painful, however, the venom is not highly toxic, and deaths from their stings have not been reported yet. Velvet ant is a parasitoid whose larvae live as parasites on immature stages of other insects, such as bees and eventually kill them. The sting is similar to bees and people who have severe allergies to the sting may show overreact to it, so contact and stings should be avoided [156-158]. Mutillidae contains about 230 genera and about 8000 species. They are distributed all over the world [159,160].

In 2014-2015, velvet ant stings caused by the Dentilla sp (Hymenoptera: Mutillidae) were reported among 49 individuals in Kashan, a city in central Iran. The majority of cases (72%) occurred in women carpet weaving workshops and inside houses, particularly in sitting rooms and bedrooms. The victims complained of severe and sharp pain, as well as redness and itching at the sting sites. In later stages, they present hemolysis and bruising manifested as brown spots. To reduce severe pain and itching in the treatment center, corticosteroids (dexamethasone), analgesics and antihistamines were prescribed Based on these findings, it was concluded that this arthropod is a domestic pest [161,162].

Formicidae family

Among these, fire ants have been identified as the primary cause of ant stings in the Qeshm Island, the largest Iranian island located in the Persian Gulf [163-168] The venom of bees and wasps is mostly composed of protein while the venom of fire ants is made up of 95% water-insoluble alkaloids [27,133,134,135]. However, it has been observed that anaphylactic shock resulting from fire ant stings exhibits similarities to anaphylactic reactions caused by bee stings.

Piperidine alkaloids are the most toxic agents in fire ant venom, causing local necrotic and hemolytic effects and being responsible for pain [27]. While some sources report a species count of 4200 along with 208 genera, it is estimated that the actual number of species may reach 6000 [169]. In Iran, 67 species from 21 different genera have been documented, with specimens collected from various provinces including Ilam, West Azerbaijan, and East Azerbaijan [170,171]. Bees, wasps, and ants are considered health pests as they frequently cause stings in both urban and rural environments. Their presence can disrupt normal outdoor activities in yards, parks, and school grounds. When provoked, they often invade residential areas, and tend to swarm, posing a threat to children and the elderly. In preparation for a swarm attack, these insects release alarm pheromones that signal other members within the colony (Figure. 4) [172,173,151,132].

Hemiptera order

The order Hemiptera contains numerous families, such as Corixidae, Notonectidae, Blastomidae, Nepidae, Pentatomidae, Reduviidae, Anthocoridae, Coreidae, and Nabidae. However, most of them are not medically important. Hemiptera, commonly known as bugs, derives its name from the Greek words "hetero-" meaning different and "ptera" meaning wings. Bugs have two pairs of wings, with the thin hind wings located under the front wings. As a result, the forewings are called Hemielytra. They possess mouthparts that resemble perforating and hypodermic needles, which enable them to extract subsurface fluids from plants and animal [174,175].

While most bug families are terrestrial, many also inhabit aquatic environments. Many bugs are vegetarian and consume plant nectar, making them

class	Order	Family	Figure	References
		Vespidae		Prepared by Dehghani R
		Formicidae		Shiran et al., (2013) with permission
Hexapoda	Hymenoptera	Mutilidae		Prepared by Dehghani R
		Apidae		Prepared by Dehghani R

Figure 4.
Stinging and venomous agents belong to Hymenoptera order (Prepared by Dehghani R)

significant pests. However, certain species are predators and are considered beneficial insects [176,177]. Several species of bugs are known to attack humans and livestock, feeding on their blood. In addition, some species are vectors for pathogens and associated with human disease [178,179]. warm regions. These insects vary in size, ranging from a few millimeters to a few centimeters. Bugs are mostly abundant in warm regions. Terrestrial species belonging to the families such as Reduviidae, Anthocoridae, Nabidae, and Coreidae pose a potential biting risk to humans [180-185]. One characteristics of terrestrial bug families is the presence of glands in both nymphal and adult stages. These glands typically produce defense chemicals known as allomones, which can vary between species but are often similar within closely related groups.

The presence of allomones is common among different species. Many Hemiptera species that inhabit soil possess special glands with ducts opening on both sides of the thorax. In defensive situations, these glands emit secretions with distinct odors. One

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example is the Pentatomidae family, which has specialized secretory glands in their thorax. Contact with the fluid emitted by these glands can cause damage to human skin [186-192].

Most species belonging to aquatic bug families are predators and have the potential to harm humans and other animals [193]. The Corixidae family is characterized by an ovoid shape and a flattened gray body, enabling them to swim deep in the water for extended periods due to the air stored under their wings. While they may resemble Notonectidae, they differ in that they are not backswimmers. Bites from Corixidae have been reported on humans, as they feed on mosquito larvae and small aquatic insects [194,195].

Bugs belonging to the Notonectidae family are commonly known as backswimmers because they swim on their backs. They typically rest obliquely on the water with their hind legs spread open. These bugs can bite humans, and their bites often result in swelling at the bite sites. The pain caused by their bite is comparable to that of a bee sting and usually lasts for 2 to 3 hours. Their dorsal surface is generally ovoid in shape and light in color. These bugs are predatory in nature, feeding on small insects and fish. They may also attack larger animals, extracting blood and bodily fluids. These insects lay their eggs on aquatic plants [196,197].

Aquatic bugs belonging to the Blastomidae family are the largest species among their kind. They have ovate and flattened bodies, reaching lengths of 5 to 8 cm, and commonly referred to as giant water bugs. They inhabit stagnant waters such as pools and lakes and are attracted to light sources, earning them the name "electric light bugs." These bugs have a brown coloration. With their specialized hunting legs, they prey on insects, snails, and even small fish. Typically, they fly to water-rich areas for hunting purposes. Their bites can cause intense and excruciating pain, posing a particular threat to children [198-200].

Bugs belonging to the Nepidae family are predators. Their front legs are modified into hunting limbs, and they possess a pair of long breathing tubes called cerci, which are as long as their bodies. These bugs have a slow-moving nature and primarily feed on aquatic animals. If handled without caution, they may bite, causing significant pain. While they possess fully grown wings, they rarely engage in flight. These insects lay their eggs inside the tissues of aquatic plants [201-206].

The aggressive and annoying behavior of these bugs, as well as their tendency to bite, is mostly triggered by catching and squeezing them. While these bugs are not typically invasive, children, in particular, are prone to bites due to their curiosity (Figure. 5). Predaceous bugs produce venom that causes rapid paralysis and liquefaction. These venoms contain highly insecticidal properties and can induce paralysis or even death if injected into vertebrates. Predatory venoms have been found to contain disulfide-rich peptides, bioactive phospholipids, small molecules such as N, N-dimethylaniline and 1,2,5-trithiepane, as well as toxic enzymes like phospholipase A2 [207].

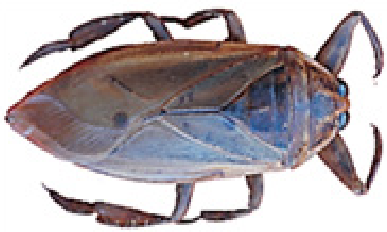
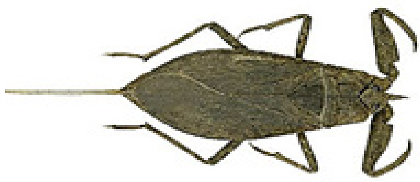
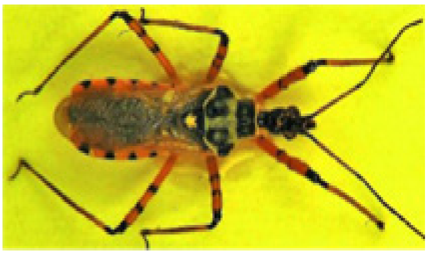
Coleoptera order

The Coleoptera order, which includes beetles and weevils, is the largest and most diverse insect order in the world. It continues to grow as new species are discovered (Figure 6). These insects exhibit a wide variety of body shapes, sizes, and colors. They are typically characterized by having two pairs of wings: a pair of modified hardened front wings called elytra, which serve as protective covers, and a second pair of membranous hind wings used for flying. Additionally, Coleoptera possess a hard outer exoskeleton, segmented antennae, and large compound eyes. Adult beetles and their larvae, known as grubs, have mouthparts adapted for chewing various materials such as other insects, fruits, nectar, leaves, fungi, dead animals, plants, and even hardwood.

Beetles play diverse and economically important roles in ecosystems due to their wide-ranging diet. In fact, beetles are known to feed on nearly every available food source in nature [208,209]. Some beetles, such as crop pests, cause damage to stored products by feeding on foodstuffs like grains and cereals. Many can also cause damage to wooden furniture, carpets, and stored food items in households. Additionally, some beetles can be problematic in gardens or agriculture as they attack plat flowers, fruits, leaves, and roots. Beetles inhabit in almost any ecosystem, ranging from the poles, deserts, lakes, ponds to underground habitats and mountain tops. Many species live in the nests of other animals and form symbiotic relationships with them.

The Coleoptera order is divided into four sub-orders: Adephaga, Archostemata, Myxophaga, and Polyphaga, comprising approximately 400,000 species. Only species belonging to the sub-order Polyphaga are poisonous. This sub-order consists of 17 superfamilies, with the most important ones being Staphylinoidea, Tenebrionoidea, and Bostrichoidea. Within these superfamilies, there are families that are both of importance to health and economy, as they can either cause harm or provide benefit to humans. These families include Staphylinidae, Meloidae, Oedemeridae, and Dermestidae.

The Staphylinidae family includes rove beetles, which are known for causing skin damage [210-212]. Also, small beetles in this family are attracted to light sources during nighttime and if they come into con-

class	Order	Family	Figure	References
Hexapoda	Aquatic bug	Belostomatidae		Jehamalar & Chandra, (2013) with permission
		Corixidae		Havemann et al., (2018) with permission
		Notonectidae		Prepared by Dehghani R
		Nepidae		Havemann et al., (2018) with permission
	Terrestrial bug	Reduviidae		Dioli et al., (2020) with permission
		Anthocoridae		Gil-Santana (2017) with permission

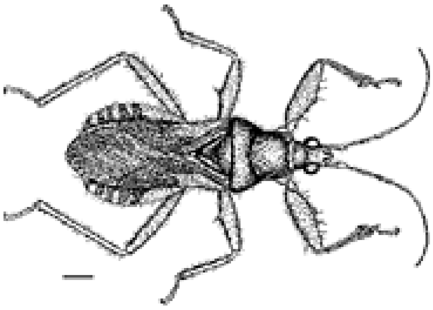
Terrestrial bug	Nabidae		Zhao et al., (2019) with permission
	Coreidae		Doughty., et al (2016) with permission
	Pentatomidae		Prepared by Dehghani R

Figure 5.
Biting and venomous agents belong to Heteroptera order (Prepared by Dehghani R)

tact with human skin, they secrete a defensive body fluid that can cause infectious blisters. It is important to note that these beetles do not bite and move slowly on the skin. However, during their movement, they release a potent poisonous compound called Paederin [213,214]. which leads to acute irritant dermatitis. This condition presents as large blisters accompanied by pain, burning sensations, and itching. There is no specific antidote or special treatment for these blisters. It is recommended not to touch or rupture them to prevent potential secondary infections. To alleviate the symptoms, immediate washing with water and soap is advised, along with the use of disinfectants and analgesic ointments. It should be noted that the healing time for these blisters is approximately 10 days or longer. While they can affect any part of the body, they are most commonly found on the face, hands, forearms, and legs [215].

In the northern region of Iran, there is an increasing prevalence of skin disorders attributed to the widespread presence of small beetles known as "Dracula" by the local population. The favorable environmental conditions, along with their high breeding and reproduction rates, have resulted in their wide distribution throughout the area. These skin problems are observed in individuals of all age groups and genders, affecting individuals from various social classes. However, it appears that the prevalence of skin disorders is particularly higher among young women [216-218].

In 2014, a 9 year old boy who had a trip to the North of Iran, was referred to the hospital due to signs of irritation on his neck skin, characterized by red plaques and blisters. He also complained of insomnia. Upon investigation, rove beetles (Coleoptera -Staphylinidae) were found in his resting place. A medical examination diagnosed him with Paederus dermatitis, which occurs as a result of contact with the hemolymph of certain rove beetles. Paederus dermatitis is a common in the northern region of Iran, primarily affecting the face, neck, and hands. Preventive measures for this condition include using mosquito nets, wearing long-sleeved clothing, and avoiding the use of fluorescent lamps. If beetles are observed on the skin, it is recommended to gently brush them away, as they do not bite but instead release a chemical toxin called Pederin, which can cause skin irritation and blistering. The treatment for the boy included quickly washing the infected area, applying cold compresses and anti-itching calamine lotion, using topical steroids, and taking oral antibiotics, and antihistamines. His recovery duration was 27 days [219]. (Dehghani et al. 2014c).

The insects of the Meloidae family inhabit arid areas, temperate steppes, subtropical and tropical savannas, as well as vast open habitats. They are found in various parts of Iran. While these beetles do not bite, their body secretion, known as Cantharidin, is venomous and can cause blisters, irritation, and burns on the skin [220-223]. (Nikbakhtzadeh and Ebrahimi 2007; Serri et al. 2012; Moslemi and Pashai Rad 2015; Nezhad-Ghaderi et al. 2021). This family, also referred to as blisters beetles, is characterized by hardened shield-like forewings or elytra. It encompasses approximately 3000 species and 120 genera worldwide [224,225]. (Bologna and Pinto 2001; Fekrat and Awal 2015). They primarily feed on plant pollen, although some of them are predators (Figure. 6).

The insects of the family Oedemeridae are commonly known as false blister beetles. Many beetles, especially those with bright colors, possess special glands that enable them to produce chemical compounds for protection against bacterial, fungal, or predatory attacks. Adult beetles of this family possess Cantharidin in their body fluids, which serves as a defense mechanism [226]. (Abtahi et al. 2012). Members of this family have a tubular body shape and display vibrant colors. When these beetles are pinched or crushed against the skin, they can cause skin lesions and blisters. While they often reside on flowers during the day, they are attracted in significant numbers to sources of light such as parks, amusement parks, and swimming pools at night, posing a potential threat to individuals (Figure. 6) [227-230].

Within the Dermestidae beetle family, there have been reports of 12 genera and 123 species in Iran. The larvae and pupae of these beetles possess specialized hairs called hastisetae, which serve as their primary defense mechanism against invertebrate and potentially vertebrate predators [231,232]. These insects feed on a variety of organic materials and their hairs can significantly contaminate stored products and environments [153]. Exposure to hastisetae can lead to allergic reactions in humans, including skin rashes, asthma, conjunctivitis, and gastrointestinal inflammation. However, little is known about the exact mechanism of action of these reactions (Figure. 6) [233-235,230].

Lepidoptera order

Lepidopterism is a term used to describe various medical conditions in humans that typically involve cutaneous and systemic reactions resulting from contact with the larval hairs or adult scales of certain butterfly species. Butterflies are insects characterized by having four wings that are typically covered in scales (Figure. 6). The larvae (caterpillars) of most butterfly species, with a few exceptions, feed on a variety of plants. Some butterfly larvae, known as stinging caterpillars, are equipped with hollow quill-like hairs that serve as defensive weapons against their natural enemies. These hairs may be connected to poison sacs containing irritating chemicals, which can cause mild itching, severe local reactions, painful blistering, or even systemic issues such as intestinal disorders. Contact with adult butterflies can also lead to skin allergies and respiratory conditions due to their scales [236-239].

A group of leaf-eating butterflies feeds on the leaves of various trees, including forest shrubs like mountain pistachio, oak, and juniper (Arjan). Their larvae are covered with fur-like hairs that, when in direct contact with human skin, can cause allergic reactions such as dermatitis, urticaria, red nodules, itching, and burning sensations. Currently, six species from four butterfly families have been identified in Iran. The larvae of these butterflies often experience periodic population peaks or outbreaks every 7 to 10 years. Some of them live in groups on their host plants and have the ability to spin silk threads and create cocoons on the trees [240,241].

Allergic reactions can occur when human skin comes into contact with the setae (hairs) and pupae (cocoon) of butterflies, or when the scales and microscopic setae from the abdomen of adult insects are inhaled. These reactions typically start with itching, burning sensations, and the appearance of red papule-like lesions measuring 3 to 7 mm. In severe cases, it can even lead to shock. During years when their population increases, these butterflies can pose problems for forest dwellers or nomadic tribes in the region. Additionally, researchers who handle these butterflies without following proper safety measures have experienced lepidopterism [242].

Envenomation resulting from contact with caterpillars is a global health issue. Any direct or indirect contact with the caterpillar's urticating hairs can lead to clinical manifestations, including localized dermatitis and potentially life-threatening systemic effects. These problems arise due to the bioactive components present in the venom of these insects, which disrupt the functioning of various organ systems in the human body. The pathophysiology of this condition is not well understood, and currently, only symptomatic relief is provided by medical professionals since there is no effective treatment available. The health and economic impacts of this problem have been underesti-

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class	Order	Family	Figure	References
Hexapoda	Coleoptera	Staphylinidae		Prepared by Dehghani R
		Meloidae		Prepared by Dehghani R
		Dermestidae		Prepared by Dehghani R
		Oedemeridae		Abtahi et al., (2012) with permission
	Lepidoptera	Saturniidae		Schowalter & Ring (2017) with permission

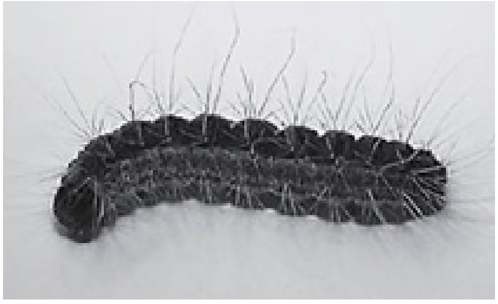
		Thaumetopoeidae		Gottschling., et al (2007) with permission
Hexapoda	Lepidoptera	Lymantriidae		Prepared by Dehghani R
		Lasiocampidae		Prepared by Dehghani R

Figure 6.
Venomous agents belong to Coleoptera and Lepidoptera orders (Prepared by Dehghani R)

mated, making it a growing concern for the future. Therefore, increasing awareness to prevent contact with these caterpillars is crucial [243-245].

Diptera order

The Diptera order, also known as true flies, encompasses a variety of flies and mosquitoes (Figure 7). Dipteran insects have mouthparts that are adapted to consume a wide range of foods, including a variety of materials such as pollen, plants, meat, feces or dung, and blood [246-249]. The Diptera order holds great medical significance as many diseases are transmitted to humans and other organisms by insects belonging to this order [250-254]. It is important to note that, despite the vast diversity and large number of species within the Diptera order, only a small percentage of them act as vectors responsible for transmitting pathogens to humans [255-258]. The Diptera order has three suborders: Brachycera, Nematocera, and Cyclorrhapha, each with numerous families. In the Brachycera suborder, three venomous families exist: Asilidae (robber flies), Tabanidae and Sciomyzidae. In the Nematocera suborder, only one venomous family, Cecidomyiidae is known. However, no venomous families have been reported in the Cyclorrhapha suborder [259].

The members of the Asilidae family, also known as robber flies, are venomous insects. Their venom contains numerous enzymes, including proteases, phosphatases, amylase, hydrolase, nucleases, and dehydrogenases. They inject their paralyzing venom into their prey while hunting, although their venom is comparatively weaker than that of spiders, scorpions, or Hymenoptera. Unlike other piercing flies that primarily feed on liquid, robber flies have independently evolved a venom delivery system. Adult robber flies produce venom in their thoracic glands and transmit it through ducts in the hypopharynx [260-262]. More than 150 species have been identified within the family of robber flies. They play a crucial role in maintaining the biological balance of insect populations because both the larvae and adults act as predators, feeding on various arthropods. Robber flies are typically active during the day (diurnal) and hunt their prey in sunny habitats. Some species within this family have developed adaptations that allow them to thrive in desert climates [263].

Tabanidae flies, commonly known as horseflies, are capable of producing paralyzing venom. In contrast to robber flies, the larvae of Tabanidae are venomous predators, while the adults feed on flower nectar or blood. Tabanidae larvae are formidable hunters that are typically active in water, on aquatic plants, and among algae. When in contact with humans, they bite, causing pain, irritation, and itching. The venom is transmitted through a channel located near the tip of the mandible. This channel is connected to a gland inside the head, which is completely separate from the feeding duct. The Tabanidae larvae inject their venom through the lower channels of the mandible [259,264]. Iran, with diverse climates, is expected to harbor a significant number of unidentified species within the Tabanidae family, which are likely to be discovered in the future [265,266 35,54].

The larvae of the Sciomyzidae family possess a potent venom composed of neurotoxins, enzymes, and small peptide molecules. This venom originates from the salivary glands of the larvae [267-269]. The larvae utilize their venom for hunting snails. When a snail is envenomated, it experiences tremors and paralysis within 60 seconds. If the snail is not consumed by the larvae, it will eventually recover as the paralysis is reversible. The recovery time depends on the duration of the bite; for example, a 15-second bite can result in one hour of snail paralysis.

In Nematocera suborder, the larvae of the Cecidomyiidae family are venomous predators. They inject venom from their salivary glands into the bodies of aphids, causing temporary paralysis for a few minutes. In Iran, 61 species belonging to 33 genera have been identified, and they are distributed throughout the country from north to south [270,271].

Neuroptera order

Species belonging to the Neuroptera order can be distinguished by characteristics such as having antennae that are clavate and long, compared to the setaceous and short antennae of Odonata (Figure 7). Many Neuroptera flies are active during the night, while others feed on wild flowers during the day, contributing to pollination. Different species of Neuroptera flies also play a crucial role in biological control by hunting small insects like aphids. Within this order, 19 families have been identified [272]. The family Myrmeleontidae, commonly known as antlions, primarily inhabit land. The larvae of this family construct conical pits as traps in sandy and loose soil. When ants fall into these inverted cones, the antlions larvae capture and feed on them [273,274].

The family Myrmeleontidae comprises more than 200 genera and over 1500 described species worldwide. Adult antlions are commonly observed flying around lights, especially during spring and summer. They possess elongated bodies, resembling dragonflies. The larvae of antlions are aggressive and active predators, characterized by their robust physique [275,276]. The antlion larvae are aggressive and active predators with strong bodies [275, 276]. They possess three pairs of legs and a narrow neck. Their small flattened head has a huge pair of sickle-like mandibles with several sharp spines. The maxillae of antlion larvae resemble hypodermic syringes, allowing them to pierce their prey's body and extract fluids. Their jaws are capable of injecting venom that aids in digesting and dissolving the contents of the prey's body. Incidents of antlion larvae biting humans are rare [277]. There has been a reported case of a rare bite occurring on the finger and arm of an elderly woman from Queensland, Australia [278].

In Iran, 97 species of antlions have been identified across various provinces, including Baluchistan, Fars, Golestan, Hamedan, Hormozgan, Kermanshah, Khorasan, and Kurdistan [279-281].

Prevention and Treatment

Arthropods' stings and bites generally result in minor trauma. However, if they deliver venom, they can cause potentially severe local or systemic envenoming. Most venomous arthropods administer their venom through a stinger, chelicerae, pedipalps, or mandibles, while others release toxic compounds from their secretory glands upon direct contact with the victim. The treatment for an arthropod sting or bite depends on factors such as the type of venom or poison involved, the quantity injected, and the overall health condition of the victim. In individuals with a history of IgE-mediated systemic allergic reactions to insect venom, self-administration of epinephrine intramuscularly (IM) into the lateral thigh should be initiated immediately to prevent potential anaphylactic reactions. Also, Venom Immunotherapy Therapy (VIT) is typically recommended to prevent allergic reactions caused by certain Hymenoptera stings. Venom immunotherapy is a treatment rather than a preventive measure. The treatment involves gradually introducing small amounts of the venom into the body in order to desensitize the immune system and reduce or eliminate the allergic response. Over time, this helps to build tolerance and prevent severe reactions in case of future stings. The decision to initiate venom immunotherapy depends on the advice of an immunologist, taking into consideration factors such as the patient's age, cardiovascular health, and the risk of allergic reactions to the treatment. However, it should be noted that approximately 1 in 10 people who undergo venom immunotherapy may experience an allergic reaction to this treatment [282-286]. Although the treatment of most insect stings and bites is similar in several aspects, each treatment may also have specific features. In the following explanation,

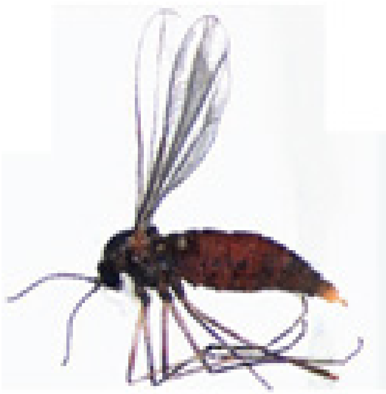
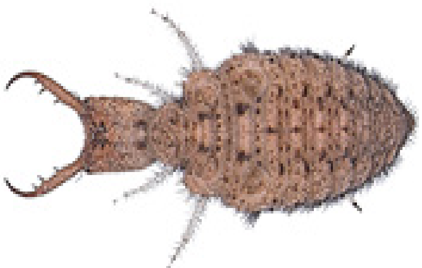
class	Order	Family	Figure	References
		Asilidae		Mohammadi et al., (2021) with permission
		Tabanidae		Prepared by Dehghani R
Diptera	Diptera	Tabanidae		Kazerani et al., (2017) with permission
		Cecidomyiidae		Schmid et al., 2018 with permission
	Neuroptera			Hajiesmaeilian et al., 2020 with permission “© Magnolia Press”

Figure 7.
Biting and venomous agents belong to Diptera and Neuroptera orders (Prepared by Dehghani R) “Neuroptera image used with permission from the copyright holder Zootaxa.

we will outline these aspects of treatment for different type of arthropods.

Scorpion venoms contain neurotoxic and cytotoxic components. The effects of scorpion stings can range from local envenoming to systemic envenoming. Approximately 50,000 cases of scorpion stings are recorded annually in Iran, mainly in the southwest region of the country. Hemiscorpius lepturus is responsible for the majority of envenoming cases and is the most prevalent species in Iran and its neighboring countries. The venom of H. lepturus primarily acts as a cytotoxic agent, exhibiting hemolytic, nephrotoxic, and hepatotoxic effects. It has been reported that the toxicity and clinical features of H. lepturus stings differ from those caused by other medically significant scorpion species [287]. The venom remains in the body, and its destructive effects manifest with a delay. Moreover, H. lepturus stings may not be easily recognizable due to their smaller size compared to other scorpions, such as the black scorpion (A. Crassicauda). In the first 24 hours, symptoms typically include minor itching and pain at the site of the sting, which many victims tend to ignore. Consequently, individuals affected by these stings often do not seek medical assistance until the main toxic symptoms become established. This delay in seeking treatment frequently results in longer hospital stays for patients in order to achieve full recovery.

Local symptoms; include cellulitis, severe inflammation, intense pain, gangrene, necrosis, swelling, and erythema at the sting site due to venom penetration into the dermis and adjacent tissues. The symptoms typically appear after 24 hours [287,288]. They can be managed with local or regional anesthesia, corticosteroids (e.g. hydrocortisone) to reduce inflammation, pain killers (e.g. acetaminophen or aspirin), and antihistamines (e.g Benadryl) [289,290,291]. In some cases, the venom may enter the blood and lymphatic systems, leading to the development of non-uniform ecchymotic patches with a diameter of up to 25 cm [287,292]. Over time, the gangrenous area may rupture, causing formation of lesions through the fatty tissue beneath the skin [287]. Extensive wounds often require skin grafts for proper healing [293-297].

Systemic symptoms; manifests as cardiotoxicity, acute kidney injury (AKI), hemoglobinuria, and CNS effects. Mental disorders can lead to cholinergic effects, such as nausea, vomiting, sweating, excessive salivation, priapism, bradycardia, hypotension, seizures, restlessness, headache, and confusion. In addition, individuals may experience adrenergic effects such as increased blood pressure, tachycardia, and heart failure [298,299]. In general, mild symptoms in adults may persist for 2 to 3 weeks without treatment [288]. The clinical treatment of systemic scorpion envenomation involves the essential use of antivenom as primary therapy [289,290,297]. In Iran, for the past 30 years, the most commonly used treatment for six common Iranian scorpions, including Androctonus crassicauda (Olivier 1807), Hottentotta (Buthotus) saulcyi (Simon, 1880), Hottentotta(Buthotus) schach (Birula 1905), Odontobuthus doriae (Thorell 1876), Mesobuthus eupeus (Koch 1839), and H. lepturus (Peters 1861), has been the administration of polyvalent antivenoms. These antivenoms are derived from equine hyperimmune serum and manufactured by the Razi Vaccine and Serum Research Institute in Karaj, Iran [292,300].

Other treatment for systemic scorpion envenomation, including standard heart failure treatment, involve the administration of inotropes along with diuretics (e.g. furosemide) to treat cardiogenic shock. Additionally, ACE inhibitors such as captopril, alpha-blockers (e.g., prazosin or doxazosin), and calcium channel blockers (e.g., nifedipine) are used to lower blood pressure [290,291,297].

In cases of low blood pressure, if necessary dobutamine, a medication used in the ICU to manage low blood pressure may be administrated. In more severe cases, excessive bronchial secretion can lead to pulmonary edema and respiratory failure. The treatment involves mechanical ventilation and the use of diuretics to manage respiratory failure [290,291,297,301, 302].

Spiders; the majority of spiders have venom that is relatively weak and often unable to cause substantial envenoming. Also, their chelicerae are usually too small to penetrate human skin. Most spider bites go unnoticed until clinical symptoms develop, and turn into local erythematous edema. Certain spiders, like brown recluse, can cause necrotic lesions, local edema, and ischemia at the bite site, leading to the gradual formation of an eschar and tissue necrosis. Other spiders, such as widow spiders, funnel web spiders, and wandering spiders, can cause systemic neurotoxic envenoming similar to scorpion stings. The clinical treatment of local venom effects is generally minor and involves routine wound care and tetanus prophylaxis. However, in severe cases with tissue necrosis around the bite site, special attention should be given the treating the necrotic tissue. In situations involving Loxosceles sp bites and systemic envenomation, specific antivenom, along with epinephrine, antihistamine, and steroids, may be necessary [288,303].

In the summer of 2017, in the city of Kashan in central Iran, a 48-year-old female cleaner was bitten by a spider while collecting garbage. The spider was later identified as a member of the Loxosceles sp (Araneae-Sicariidae). The initial symptoms she experienced included immediate irritation, itching, swelling, redness on her arm and numbness in three of her fingers. She also suffered from shortness of breath. After four days, her hand became edematous and painful, and she also experienced insomnia. Her condition worsened to the point where she lost the ability to move her fingers. Due to the severity of her condition, she was hospitalized for four days and received various treatments including normal saline, corticosteroids (dexamethasone), antibiotics, antihistamines, and analgesics. Additionally, she was administered a tetanus vaccine and tetabulin [42].

Ticks; the first step in the treatment of tick bites is to remove the attacker's tick with fine-tipped tweezers to grasp the tick at the level of the skin to remove the tick, particularly the head and mouthparts. Then thoroughly clean the bite site with soap and water, and apply alcohol or an iodine scrub to prevent infection. A dose of antibiotics may need to prevent accruing of tick-borne diseases like Lyme disease. If symptoms of paralysis appear, respiratory function should be monitored closely. In severe cases, mechanical ventilation at the ICU level may be required [304-306]. It should be noted that, researchers have been studying various approaches to develop vaccines against ticks that involves identifying specific proteins or molecules found in ticks that play crucial roles in their life cycle or ability to transmit diseases, then isolate and purify these proteins and use them to create a vaccine [71].

Hymenopterian sting treatment options, the result of the most Hymenopteran stings are uncomplicated and limited to local inflammation in a small area. They typically present with focal edema, warmth and redness, which usually recover within a few days. However, in cases when multiple stings occur or in large local reactions (10 cm or more), more severe symptoms such as erythema, induration, increased warmth, intense pain, and longer persistence may be observed.

Systemic consequences resulting from immediate hypersensitivity reactions and anaphylaxis, can be fatal, and needs early medical intervention. Symptoms include difficulty breathing, wheezing, generalized urticaria, angioedema, flushing, and hypotension or even shock. The therapeutic approach includes prescribing a wide range of medicines along with necessary therapeutic measures based on the type of reactions to stings. Before any pharmacological treatment, the stinger should be removed via scraping with a credit card (or like that) rather than squeezing to avoid further venom injection. After that, ice packs should be applying to reduce pain. For uncomplicated local reactions, common prescriptions include non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen for pain relief, as well as H1/H2 blockers/antihistamines, such as diphenhydramine and normal saline. In patients with large local reactions, the same treatment is administrated along with glucocorticoids, such as prednisone, at doses of 40 to 50 mg/kg for 3-5 days [134,307].

Systemic reactions, such as anaphylaxis, present with generalized urticaria, angioedema/facial swelling, stridor, respiratory distress/wheezing due to bronchospasm, abdominal pain, nausea, vomiting and flushing. For treatment of systemic reactions, monitoring the function of respiratory system is crucial because the airway can be compromised within seconds to minutes. Therefore, early intubation may be necessary. For anaphylactic reactions, life-saving administration of epinephrine is essential. The recommended dose is 0.3-0.5 mg administered intramuscularly (IM), and it can be repeated every 5 to 15 minutes if needed. Corticosteroids (such as prednisone, methylprednisolone, or dexamethasone) should be given to reduce inflammation. Additionally, antihistamines such as diphenhydramine (Benadryl), should be administered to alleviate pruritus, erythema, and urticaria. Intravenous (IV) fluids (isotonic crystalloids) at doses of 10-20 ml/kg, should be provided immediately [134,307, 308].

Bees, wasps, Fire ants and Velvet ants, the stings of honeybees and wasps can be dangerous for allergic individuals. True envenoming is rare and typically requires hundreds of stings in adults. Unlike allergic reactions, only 5% of all deaths are caused directly by their venom. The first step in treating a bee sting is to remove the stinger as quickly as possible because it continues to pump venom into the skin even after detaching from the bee's body [309].

In most non-allergic patients, a single sting may only cause local inflammation, pain, redness, and swelling as the main clinical symptoms. However, multiple stings can lead to extensive swelling, which can result in hypovolemia, hemolysis, neurological disorders, myolysis, and renal failure. Immediate hypersensitivity and anaphylaxis reactions pose the most significant risk associated with hymenopteran stings and can be life-threatening. Within minutes after a sting, systemic symptoms such as tachycardia, flushing, abdominal colic, or diarrhea may appear. Without effective treatment, these symptoms can progress to hypotension, coma, and even death [307,309]. The standard clinical treatment involves administration of adrenaline, steroids, and antihistamines to counteract allergic reactions. For patients experiencing sting anaphylaxis, adrenaline (0.1%) is life-saving intervention given at doses of 0.5–1.0 ml for adults, and 0.01 ml/kg for children, administered intramuscularly (IM). In allergic and non-allergic individuals, local wound management and tetanus prophylaxis are applied if necessary [309]. Fire ant, (Hymenopteran) stings may cause serious health problems in highly sensitive individuals and causes nausea, vomiting, diarrhea, and even difficulty breathing and emergency hospilatisation. Generally, Fire ant stings are treated symptomatically with antihistamines (e.g., Benadryl) or a similar over-the-counter oral antihistamine, topical corticosteroids (e.g., hydrocortisone ointment), and cold compresses, which can effectively alleviate pain and reduce localized reactions [155,167,310].

Over-all, systemic analgesics such as ibuprofen or paracetamol (acetaminophen) are recommended for pain control, and intense itching of bite site [125,123]. Velvet ants; Symptoms of a velvet ant stings typically include minor local reactions such as pain, swelling, and redness, which are generally not life-threatening. The treatment involves removing the sting, if present, using a similar method to that used for removing a bee sting. The sting site should be cleaned with soap and water, and applying a cold compress to alleviate pain and reduce swelling. If necessary, over-the-counter pain relievers such as ibuprofen or acetaminophen can be used. To relieve itching, topically applying calamine lotion is effective. It is important to keep the sting site clean, in order to prevent skin infections. Additionally, using zinc oxide ointment can aid in healing the irritated skin. Furthermore, administration of an antihistamine such as Benadryl or Claritin can help counteract histamine reactions at the bite site [166,162,163].

Beetles and Miilipede; the Beetles of the families Staphylinidae, Meloidae, Oedemeridae, Dermestidae, and species of Millipede class, release their chemical toxin upon contact with the victim, therefore, before applying any medicinal treatment such as topical steroid ointments, it is recommended to wash the affected area with soap and water as soon as possible. Additionally, irrigation with alcohol or ether can be beneficial. In the case of contact with larvae of Lepidoptera, oral antihistamines and topical corticosteroids are commonly used for treatment [81,116,310]. For centipedes' bites, it is recommended to wash the bite site with soap and clean water and apply a cold compress.

Bugs; aquatic bugs are the primary biting insects in the Hemiptera order. Their bites are very painful, and if scratching occurs, the bite site may become infected. The treatment for aquatic bug bites is generally symptomatic [310].

Conclusion

This study highlights the widespread presence of venomous and poisonous arthropods across Iran and its neighboring countries, an area that has received insufficient attention regarding their significance in various scientific disciplines. It is suggested to entomologists and biologists to intensify their efforts in species identification, behavioral studies, and understanding the biology and dispersal of these organisms, as well as their implications for human health and the environment. Increased awareness and knowledge of these species will equip professionals to respond more effectively to natural and accidental incidents, particularly in emergency situations.

The study also provides a comprehensive list of biting and stinging venomous arthropods in Iran and the broader Middle East, emphasizing the need for physicians and healthcare staff to recognize the medical significance of these species, assess the severity of their bites or stings, and implement appropriate patient management strategies. Currently, the educational framework for medical staff regarding the risks associated with arthropod and other venomous animal bites is lacking. Therefore, it is crucial for health policymakers at both national and regional levels to prioritize these issues and integrate them into academic curricula to enhance preparedness and response capabilities in healthcare settings.

Authors' Contributions

R. Dehghani study conception and design. R. Dehghani, M. Dehghani and N. Mohammadzadeh were contributed in Material preparation and, data collection. The first draft of the manuscript was written by R. Dehghani and B. Fathi and all authors commented on previous versions of the manuscript. B. Fathi critically revised, edit and submitted the manuscript. Finally, all authors read and approved the final manuscript.

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Conflict of interest

The authors do not have conflict of interest.

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