

Characteristics of Venomous Coleopterans and Their Venom with Therapeutic Power (Insecta: Coleoptera)

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<p>Abstract: The medical importance linked to these beetles is because they have a terpene in their hemolymph insect blood that is soluble in various organic solvents, but practically insoluble in water, cantharidin. Only synthesized male cantharidin is stored until mating and transferred to the female at the time of copulation. When molested, these insects expel the toxin through the membranous joints of the body, causing vesicles similar to burns on human skin. Meloid beetles generate a poisonous chemical compound to, among other things, defend themselves from their predators. An international research team involving the Complutense University of Madrid has shown that cantharidin is toxic to several common parasites. The results explain that some birds, such as the great bustard, ingest this type of beetle, among other beneficial properties, due to the antiparasitic activity of cantharidin. The objective of this manuscript was to describe the characteristics of venomous coleopterans and their venom with therapeutic power (Insecta: Coleoptera). This is a narrative review of the literature, which is indicated to explain and discuss a certain subject from a theoretical or contextual perspective, in a to allow the reader to acquire and/or update knowledge on a specific topic. The search for scientific articles that made up this review was carried out on Google Scholar, Biological Abstract, HAL, Qeios, ResearchGate, Scielo, and SSRN. The following descriptors in Health Sciences (DeCS) were used: biological therapy, larva, wound, debridement, and healing. The following inclusion criteria were considered: Original articles and reviews, published nationally and internationally in full, available electronically, and published in Portuguese, English, and Spanish. The exclusion criteria were dissertations, theses, monographs, and conclusion work, duplicates, and those that required payment to access the content in full.</p> <p>Keywords: Antimicrobial, Antifungal, Antitumor, Beetle, Medical Importance, Pest.</p>	<p>Research Paper</p>
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1. INTRODUCTION

Coleoptera are insects popularly known as beetles and can be found in almost all environments. What defines whether the insect is of this order is the presence of the elytra, which are the first pair of wings, those hard structures that are resistant to great pressure and impacts, protecting its entire body. The elytra function as rigid cases for the second pair of wings, which in turn are membranous and delicate. So, when beetles fly, they first open the elytra, and then the second pair of more membranous wings that are found underneath the elytra, which is what propels the flight (Figure 1) (Gullan and Craston, 2008; Amaral *et al.*, 2018; Valencian Government, 2018; Amaral, 2019; Rafael *et al.*, 2024).

1.1. Characteristics of Coleoptera

Coleoptera are characterized by presenting great morphological variability, a characteristic that has allowed them to colonize all types of environments and habitats, from freshwater to marine environments. This has made them the most evolutionary successful group of animals. But what are Coleoptera like? These are the main characteristics of Coleoptera. Like insects, the body of Coleoptera has three characteristic tagmas: the head, the thorax, and the abdomen. However, the existence of a prothorax covered by the elytra (fully hardened modified wings with a protective function for the second pair of wings, the posterior part of the thorax, and the abdomen), gives the sensation that the body is divided into an anterior part, formed by the head and prothorax, and a posterior one under the elytra (Figures 2 & 3) (Gullan and Craston, 2008; Amaral *et al.*, 2018; Valencian Government, 2018; Amaral, 2019; BASF, 2020; Assef, 2023; Rafael *et al.*, 2024).

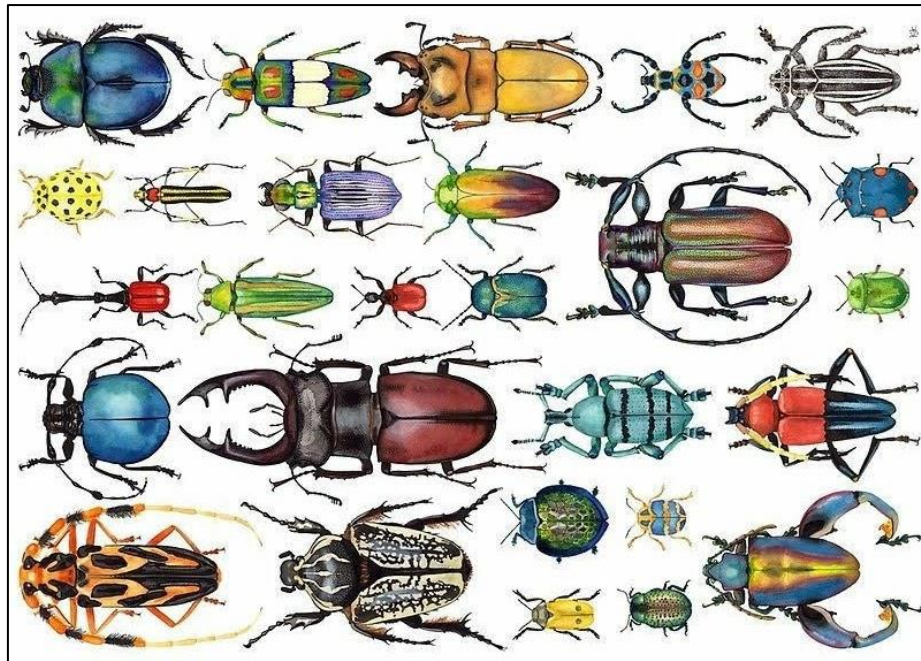


Figure 1: Diversity of the Order Coleoptera

Source: https://www.naturezapeculiar.com/2020/05/a-ordem-coleoptera.html#google_vignette



Figure 2: The life cycle of the Japanese beetle, including (a) eggs David Cappaert, Michigan State University, www.forestryimages.org, (b) larvae (grubs) David Cappaert, Michigan State University, Bugwood.org, (c) pupa (USDA-APHIS), and (d) adult

Source: Theresa Cira, University of Minnesota

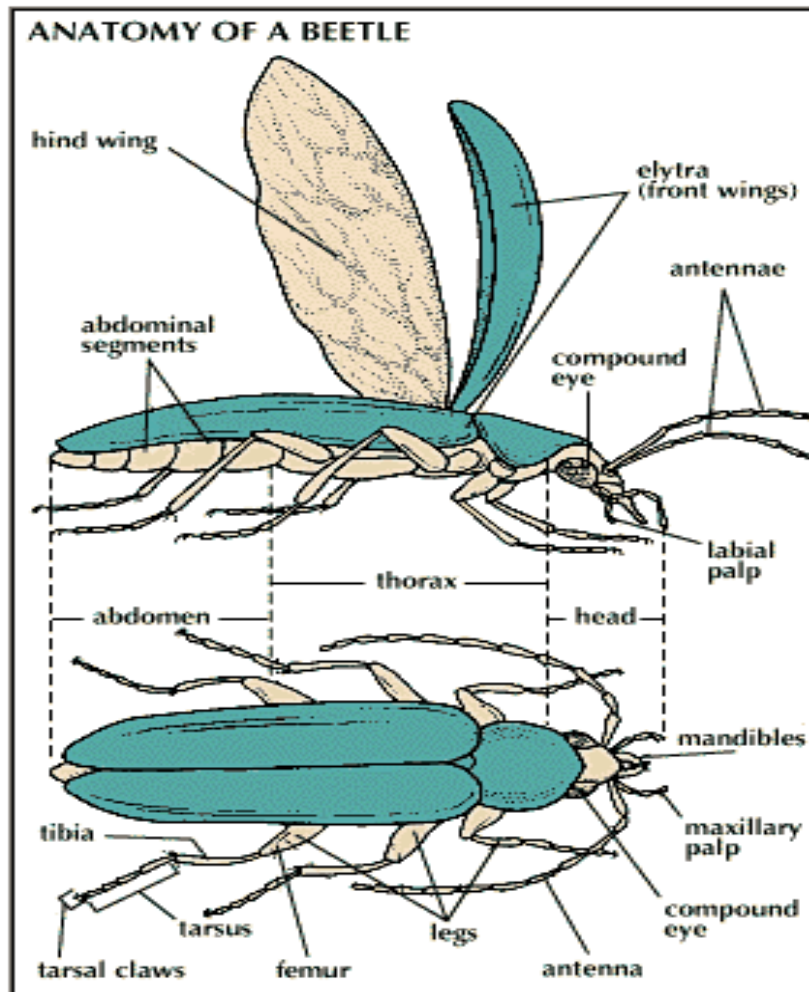


Figure 3: External morphology of the Order Coleoptera
 Source: <https://kids.britannica.com/students/article/beetle/273149>

Commonly, the head is prognata, that is, the longitudinal axis of the rest of the body coincides with that of the head. It is equipped with a cephalic capsule, where the following regions are distinguished: the forehead, the vertex between the forehead and the occiput, and lateral areas known as genas, where the compound eyes are located. In this capsule, a pair of antennae and the mouthparts are connected, the latter provided with an orthopteroid structure that facilitates chewing (Amaral *et al.*, 2018; Valencian Government, 2018; Amaral, 2019; BASF, 2020).

1. The thorax is characterized by a clear division into prothorax and pterothorax. The first section is free while the second forms a functional unit. The metathoracic wings are membranous and fold transversely below the elytra, being normally longer than these.
2. The abdomen is divided between ten or eleven segments, of which the visible sternites are 5 or 6 (corresponding to segments III to VII or VIII).
3. Regarding the size of the individuals, this usually ranges between 0.3 mm for some Ptiliidae and 200 mm for the females of *Titanus*

4. *giganteus* (Linnaeus, 1771), and *Xixuthrus heros* (Gräffe, 1868) (Cerambycidae).
5. Due to the extreme diversity of this order, we can find different types, colors, and behaviors, some being colorful, with spots, large and small. They play a fundamental role on the planet, contributing to the ecological balance of life, the food chain, and sources of scientific research, they are bioindicators of impacts caused by humans and pollinators and for controlling pests in agriculture (Amaral, 2019; BASF, 2020; Assef, 2023; Rafael *et al.*, 2024).
5. Most species are phytophagous and feed on practically all parts of the plant, roots, leaves, flowers, fruits, and pollen, however, they can be carrion scavengers, excrement coprophages, predators, parasites, or can even infest stored animal or vegetable products. In the aquatic environment, characteristics of Coleoptera such as scavengers, fungus feeders, phytophagous parasites of vertebrate animals, predators, and parasitoids of other insects. The Coleoptera is made up of around 350 thousand species, which represents 40% of all insects and 30% of

animals, forming the largest group of organisms on Earth. In Brazil, approximately 28 thousand species belonging to 105 families are recorded (Figure 4) (Gullan and Craston, 2008; Amaral

et al., 2018; Valencian Government, 2018; Amaral, 2019; BASF, 2020; Assef, 2023; Rafael *et al.*, 2024).

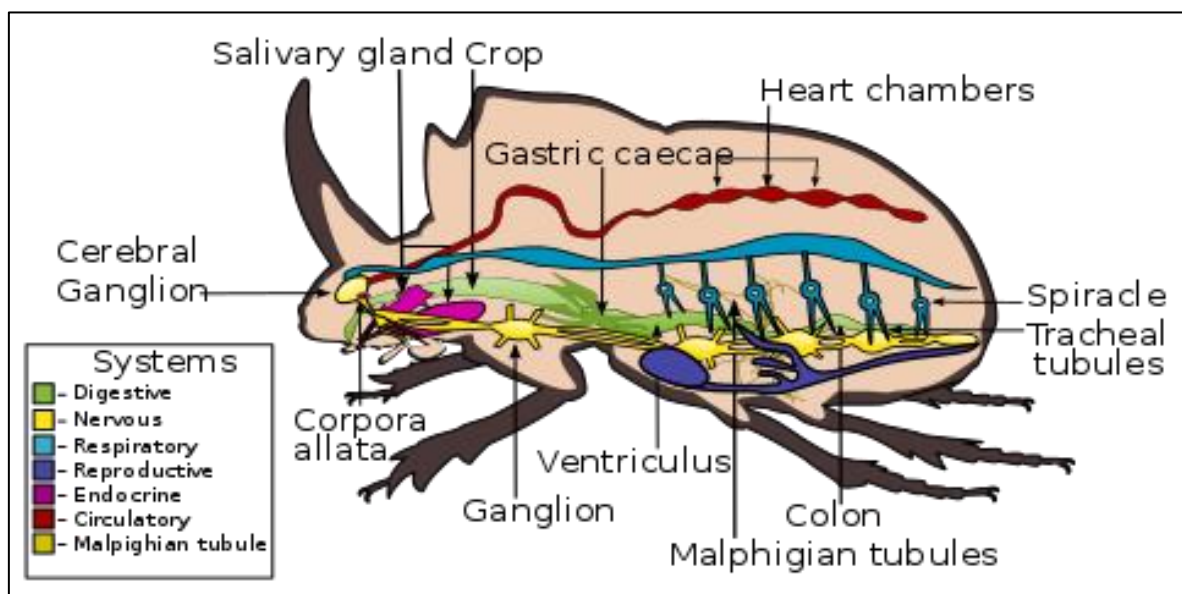


Figure 4: Internal morphology of the Order Coleoptera

Source: https://commons.wikimedia.org/wiki/File:Internal_morphology_of_Coleoptera.svg

2.0. Objective

The objective of this manuscript was to describe the characteristics of venomous coleopterans and their venom with therapeutic power (Insecta: Coleoptera).

3.0. METHODS

This is a narrative review of the literature, which is indicated to explain and discuss a certain subject from a theoretical or contextual perspective, in a to allow the reader to acquire and/or update knowledge on a specific topic. The search for scientific articles that made up this review was carried out on Google Scholar, Biological Abstract, HAL, Qeios, ResearchGate, Scielo, and SSRN. The following descriptors in Health Sciences (DeCS) were used: biological therapy, larva, wound, debridement, and healing. The following inclusion criteria were considered: Original articles and reviews, published nationally and internationally in full, available electronically, and published in Portuguese, English, and Spanish. The exclusion criteria were dissertations, theses, monographs, and conclusion work, duplicates, and those that required payment to access the content in full.

4.0. Poisonous Beetle

Coleoptera of medical importance in Brazil, accidents by beetles of the genus *Paederus* Fabricius, 1775 (Coleoptera, Staphylinidae) are described in the

Norte, Northeast, and Central-West regions and by the genus *Epicauta* Dejean, 1834 (Coleoptera, Meloidae) in the State of São Paulo. The genus *Paederus* comprises small besoums with an elongated body, measuring 7 to 13 mm in length they have short rhythms, which leave more than half of the abdomen uncovered. They live in humid places, rice fields, and corn and cotton crops (Cardoso *et al.*, 2003; France *et al.*, 2009; Jenner and Undheim, 2017; Monaco, 2017).

4.1. Family Meloidae and Therapeutic

The size of meloids varies from 15 to 35 mm. The coloring is in most cases dark brown or black. Adult meloids generally destroy useful plants such as potatoes, tomatoes, and beets. The most common species in our fauna belong to the genus *Epicauta* and are popularly called vaquinha, donkey, papa-pimenta, and póto-grande. The medical importance linked to these beetles is because they have in their hemolymph insect blood a terpene that is soluble in various organic solvents, but practically insoluble in water, cantharidin. Only males synthesize cantharidin, which is stored until mating and is transferred to the female at the time of copulation. When molested, these insects expel the toxin through the membranous joints of the body, causing vesicles similar to burns on human skin (Figure 5) (Cardoso *et al.*, 2003; Costa and Ide, 2006; France *et al.*, 2009; Monaco, 2017; Assef, 2023; Camargo, 2024; Rafael *et al.*, 2024).

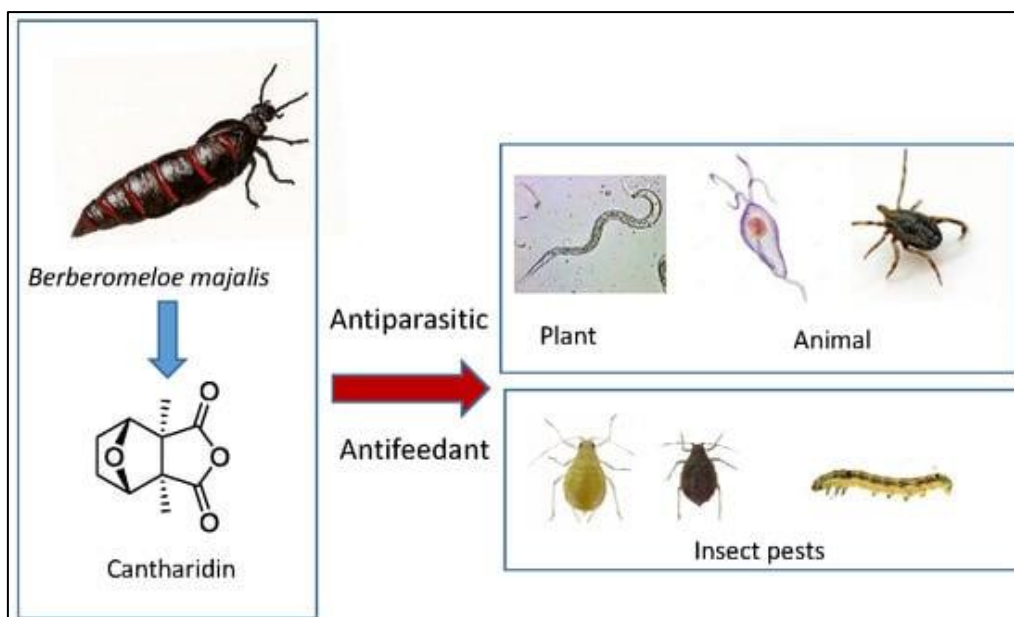


Figure 5: Antiparasitic properties of cantharidin and the blister *Berberomeloe majalis* (Linnaeus, 1758) (Coleoptera: Meloidae)

Source: <https://doi.org/10.3390/toxins11040234>

Scientific Name: *Lytta vesicatoria* (Linnaeus, 1758) (Coleoptera: Meloidae)

Measuring 1 to 2 cm, this beetle lives in southern and central Europe, Siberia, and North America. It starts to appear in Europe during the summer. The female lays her eggs close to the bees, so when the babies are born, they enter the bees' nest. Inside they undergo a transformation, they shed their skin and

become tiny larvae that start to feed on the bee's babies. In addition to giving off a very strong smell, so that predators do not approach them, they release a poison that burns the skin, forming blisters. This is among the most venomous beetles that exist (Figure 6) (Cardoso *et al.*, 2003; Costa and Ide, 2006; France *et al.*, 2009; Monaco, 2017; Whitman *et al.*, 2019; Assef, 2023; Camargo, 2024; Rafael *et al.*, 2024).

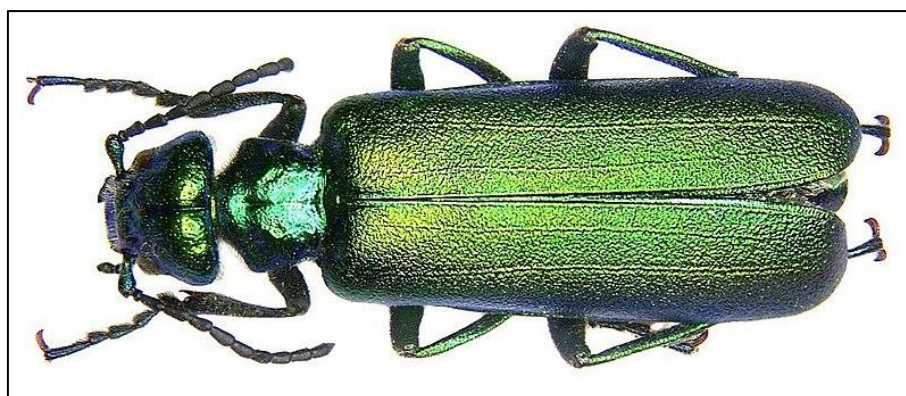


Figure 6: *Lytta vesicatoria* (Linnaeus, 1758) (Coleoptera: Meloidae)

Source: https://commons.wikimedia.org/wiki/File:Lytta_vesicatoria_%28Linn%C3%A9,_1758%29.jpg

4.2. Family Staphylinidae

The beetles of this family are elongated and between 1 and 10 mm in length. The abdomen is completely exposed, with the elytra front wings being small, blue, or bright green. The Staphylinidae that cause accidents belong to the genus *Paederus* it causes burns and even pustules when it comes into contact with the skin. Very common in the North and Northeast of the country, the insect population increases after the rainy season and arrives in cities attracted by the light emitted

by lamps). They are found in plantations of beans, potatoes, cotton, sugarcane, corn, and grasses along riverbanks. *Paederus* has two sacs near the anus, which expel a vesicant secretion, producing burns on human skin. The acidic substance of *Paederus* is more active than the cantharidin of the meloids (Figure 7) (Cardoso *et al.*, 2003; Costa and Ide, 2006; France *et al.*, 2009; Monaco, 2017; Assef, 2023; Camargo, 2024; Rafael *et al.*, 2024).



Figure 7: genus *Paederus* Fabricius, 1775 (Coleoptera, Staphylinidae)

Source: From Bouchard (2014) and <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/paederus>

Five species of *Paederus* Fabricius, 1775, are associated with human accidents in Brazil: *Paederus amazonicus* Sharp, 1876, *Paederus brasiliensis* Erichson, 1840, *Paederus columbinus* Castelnau, 1835, *Paederus fuscipes* Curtis, 1826, and *Paederus goeldi* Wasmann, 1905. They are polyphagous species, predators of other insects, nematodes, and tadpoles. When molested, adults defend themselves with their jaws, trying to bite at the same time as they bend their

abdomen, they probably also trigger the secretion of the pygidial glands. The genus *Epicauta* Dejean, 1969 (Coleoptera, Meloidae), the cantárids of the New World also endowed with vesicant properties attributed to cantharidin causing less obvious lesions, which resolve in about three days (Figure 8) (Kellner and Dettner, 1995; Costa and ide, 2006; Machado, 2007; Panta and Poudyal, 2013; Taneja *et al.*, 2013; Silva, 2015; Monaco, 2017; Vujisić *et al.*, 2020).

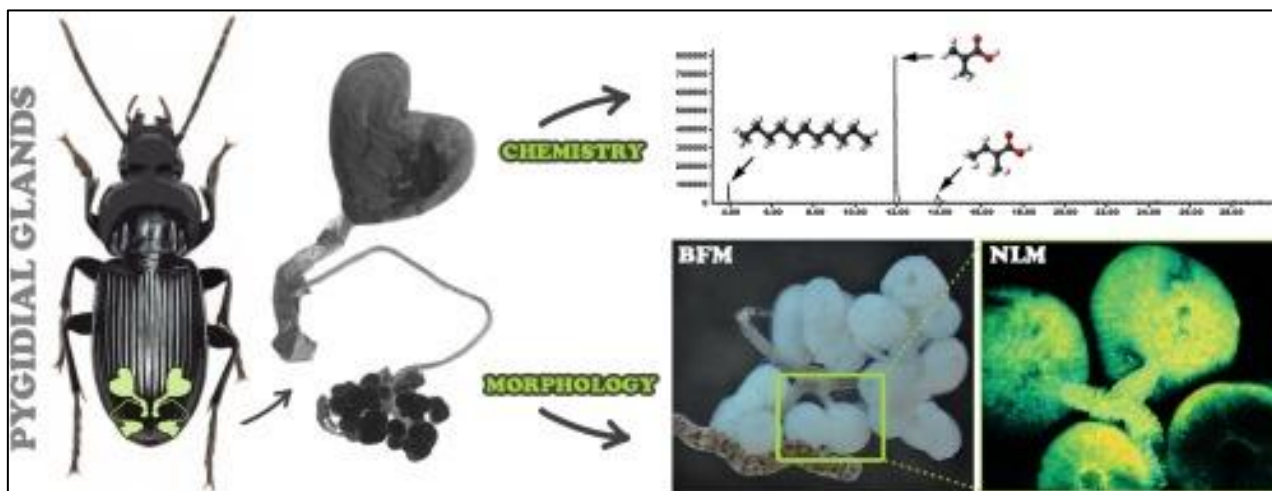


Figure 8: Chemistry and morphology of the pygidial glands

Source: DOI: 10.15226/2378-1726/7/2/001112

Some patients experience a continuous burning sensation upon contact. The clinical picture varies in intensity, and the accident can be classified as: a) Mild: mild edema. onset approximately 24 hours after contact, which persists for approximately 48 hours. b) Moderate: marked erythema, burning, and itching, also beginning a few hours after contact. A vesicular stage ensues, the lesions gradually spreading until they reach maximum development in around 48 hours (Kellner and Dettner, 1995; Costa and Ide, 2006; Machado, 2007; Panta and Poudyal, 2013; Taneja *et al.*, 2013; Silva *et al.*, 2015; Monaco, 2017; Amorim *et al.*, 2020).

A scaly stage then appears: The vesicles become umbilicated, dry for about 8 days, and exfoliate, leaving pigmented spots that persist for a month or more. c) Severe: generally, more extensive due to contact with several specimens, with additional symptoms, such as fever, and local pain. Vxtymgia and vomiting, the erythema may persist for months. The lesions are typically elongated, due to the insect rubbing on the skin. Hence the expression linear dermatitis. The vesicles may be clear or pustulized due to secondary infection. The most exposed areas of the body are the most damaged. The palms of the hands and soles of the feet appear to be spared (Figure 9) (Kellner and Dettner, 1995; Costa and

Ide, 2006; Machado, 2007; Panta and Poudyal, 2013; Taneja *et al.*, 2013; Silva, 2015b, Monaco, 2017).

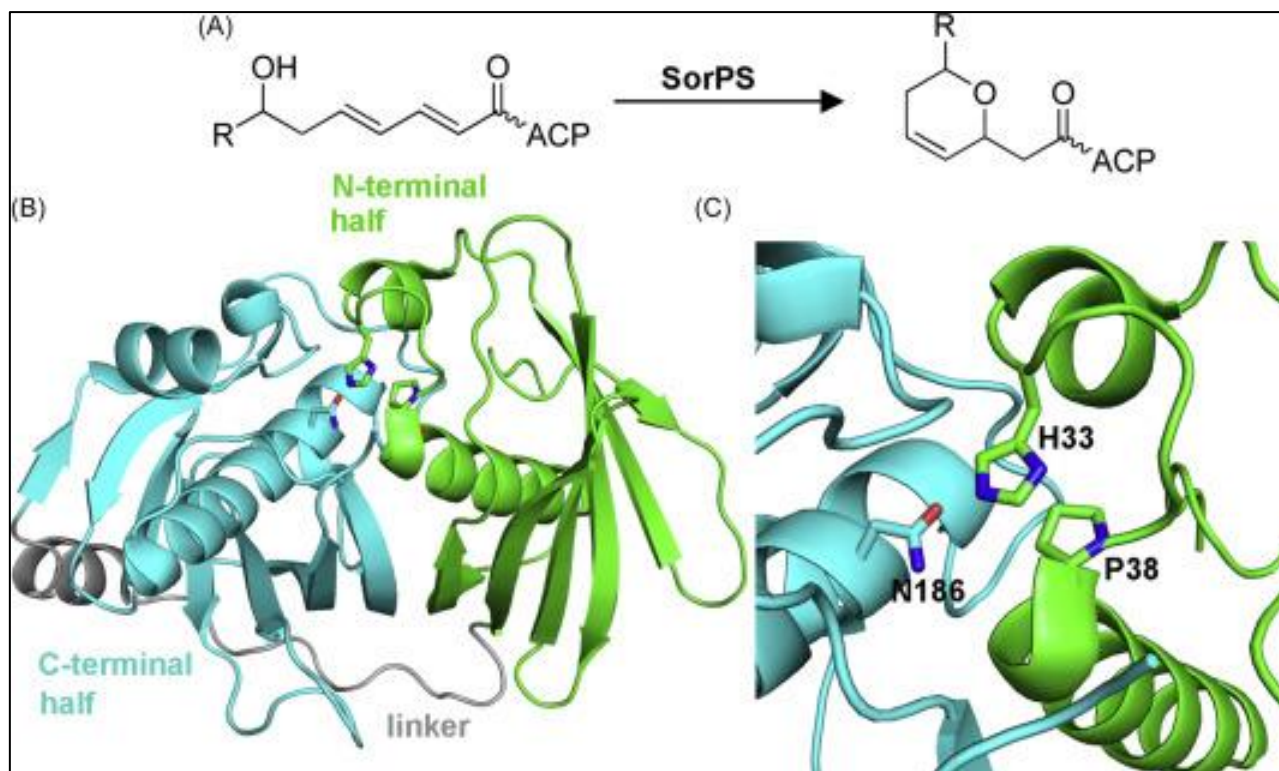


Figure 9: Pederin structure of PS domain. (A) The PS domain catalyzes the formation of five- or six-membered cyclic ether. (B) The PS domain forms a double-hotdog overall fold. (C) The active site of SorPS9. The catalytic H33 is in an Hx4P motif that replaces the conserved DH Hx8P motif. The N186 replaces the conserved DH aspartate. Catalytic residues are shown as sticks. The H33 is proposed to transfer the proton between ether oxygen and $C\alpha$ following the attack of $C\beta$ by hydroxyl at ζ position

Source: Advanced Fiber-Reinforced Alkali-Activated Composites, 2023

Several toxins cause the lesions caused by potó, the most important being pederine, belonging to the group of cyclic amides. This substance can block the production of proteins in mammalian cells, disrupting the process of mitotic cell division, and deoxyribonucleic acid synthesis, and stopping the formation of mitosis. Skin lesions caused by the potó beetle *Paederus* sp. They are known as pederism or linear dermatitis, due to how the victim presses the insect on the skin, generally dragging it with their hands and leaving a linear trail (Kellner and Dettner, 1995; National Health Foundation, 1998; Gupta, 2014; Taneja *et al.*, 2013; Jenner and Undheim, 2017).

Dermatitis, inflammation of the skin caused by potó, appears as an acute reddish erythematous lesion with slow and spontaneous resolution, disappearing after

weeks. The injuries can be roughly compared to what happens when a drop of hot or caustic liquid accidentally hits human skin, but they are poisonings that cause vesicles and blisters, not burns. There is no specific treatment. As pederin slowly penetrates the skin, after contact with the insect, it is suggested to wash the areas suspected of being caused by the insect with soap and water to neutralize the vesicant action of the insect. In general, professionals treat potó feathering injuries with a mixture of water, glycerin, talc and zinc oxide, and wads of hydrophilic gauze containing a solution of potassium permanganate or magnesia sulfate (Figure 10) (Kellner and Dettner, 1995; National Health Foundation, 1998; Costa and ide, 2006; Machado, 2007; Taneja *et al.*, 2013; Gupta, 2014; Jenner and Undheim, 2017; Amorim *et al.*, 2020).



Figure 10: A more detailed view of the lumbar plaque, with 2 bullous lesions on the extremities and 2 central eroded areas

Source: DOI: 10.15226/2378-1726/7/2/001112

In more severe cases, treatment based on topical or oral corticosteroids is necessary. Antibiotics may be necessary if secondary infections occur due to scratching the affected areas. In case of contact with the eyes, wash the area with plenty of clean water. In Egypt, eye injuries are treated with medications targeting eye inflammation sensitive to steroids or at risk of bacterial eye infection topical use (Costa and Ide, 2006; Brazil, 2024; Camargo, 2024).

5.0. How to prevent accidents

- 5.1. Screen doors and windows.
- 5.2. Swap white lights for yellow ones.
- 5.3. Sleep under a mosquito net.
- 5.4. Avoid using white bedspreads.
- 5.5. Turn off yard and porch lights to prevent insects from being attracted.
- 5.6. Be careful with waste, as potós feed on decomposing organic matter.
- 5.7. Remove excessive tree vegetation around the residence.
- 5.8. Wear gloves and a long-sleeved shirt when carrying out rural activities (Machado, 2007;

Taneja *et al.*, 2013; Brazil, 2024; Camargo, 2024; Rafael *et al.*, 2024).

6.0. Family Cerambycidae

Cerambycidae (Coleoptera), with approximately 35,000 species described worldwide. The majority, in the larval stage, are composed of phytophagous species with a broad spectrum of food sources, mainly dead wood, but they can also occur in live plants, seeds, and roots. With this type of feeding habit, cerambycids play a very important role in recycling dead plant matter, reducing it to powder, while the galleries opened by the larvae facilitate the penetration of water and decomposer microorganisms into the wood. On the other hand, these insects cause damage when they inhabit the agroecosystem and attack plants of agricultural interest and human health (Figure 11) (National Health Foundation, 1998; Costa and Ide, 2006; Machado, 2007; Taneja *et al.*, 2013; Panta and Poudyal, 2013; Brazil, 2024; Camargo, 2024; Rafael *et al.*, 2024).

Onychocerus albitarsis Pascoe, 1859 (Coleoptera: Cerambycidae).

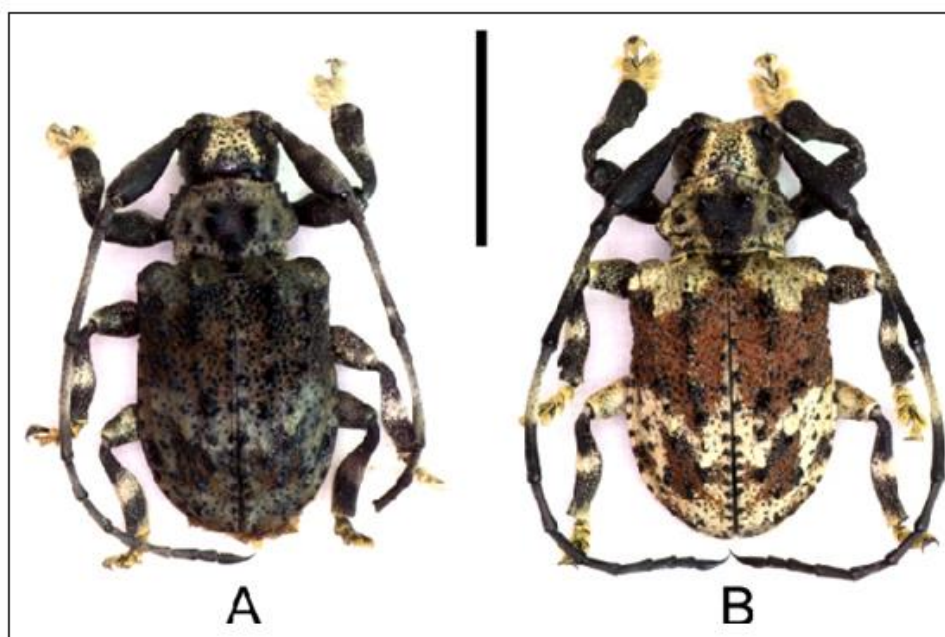


Figure 11: *Onychocerus albitarsis* Pascoe, 1859 (Coleoptera: Cerambycidae). Specimens collected of cases 1 (A) and 2 (B). The scale bar equals 1 cm

Sources: DOI: 10.4172/2161-0495.1000392Corpus and ID: 80897370

Onychocerus albitarsis is a neotropical insect of the order Coleoptera and the family Cerambycidae, subfamily Lamiinae; a beetle whose habitat is the humid tropical and subtropical forests of South America; from the Amazon River basin and Atlantic Forest of Brazil to southern Peru, Bolivia and Paraguay. In Brazil, there are records for the states of Amazonas, Maranhão, Ceará, Bahia, Goiás, Mato Grosso, Minas Gerais, Espírito Santo, Rio de Janeiro, São Paulo and Paraná. It is the only known beetle with antennae equipped with toxin inoculators and can inject such chemical compounds when under predation or when they feel threatened. They feed on plants from the Anacardiaceae and Euphorbiaceae families, which include among their members species with toxicity that could be included in their venom production process (National Health Foundation, 1998; Panta and Poudyal, 2013; Gupta, 2014; Brazil, 2024; Camargo, 2024; Rafael *et al.*, 2024).

7.0. Therapeutic Action

7.1. Beetle Venom has Antiparasitic Properties for Bustards

Meloid beetles generate a poisonous chemical compound to, among other things, defend themselves from their predators. An international research team involving the Complutense University of Madrid has shown that cantharidin is toxic to several common parasites. The results explain that some birds, such as the great bustard, ingest this type of beetle, among other beneficial properties, due to the antiparasitic activity of cantharidin. (France *et al.*, 2009; Jenner and Undheim, 2017).

Cantharidin, a toxin generated by the common oilseed insect *Berberomeloe majalis* Linnaeus, 1758, has antiparasitic and antimicrobial properties for the bustards that feed on them, according to international research in which the Complutense University of Madrid (UCM) participates. In addition to being a source of nutrients and energy, ingestion of this type of beetle serves as a shield for bustards against parasites such as protozoa, helminths, and arthropods (France *et al.*, 2009; Monaco, 2017; Yan, *et al.*, 2023).

“In this work, the ixodicidal, nematocidal and antiprotozoal activity of an extract of this beetle was studied in detail, presenting very interesting and hitherto unknown results”, (says Alexandra Ibáñez Escribano, a researcher at the UCM Faculty of Pharmacy and one of the authors of the published work in Toxins). To carry out the study, the researchers prepared extracts from the beetle's body, with the hemolymph, a circulatory fluid similar to the blood of invertebrates that contains cantharidin, and with cantharidin synthesized in the laboratory (Cardoso *et al.*, 2003; France *et al.*, 2009; Monaco, 2017; Assef, 2023; Rafael *et al.*, 2024).

The activity of each extract was tested against the parasites *Trichomonas vaginalis* Donné, 1836 (Zoomastigopora: Trichomonadidae; Trichomonadidae), *Meloidogyne javanica* (Treub, 1885) (Nematoda: Tylenchida: Heteroderidae), *Hyalomma lusitanicum* Koch, 1844 (Arachnida: Ixodida: Ixodidae), *Myzus persicae* Sulzer, 1776 (Hemiptera: Aphididae), and *Rhopalosiphum padi* L., 1758 (Hemiptera: Aphididae) (Figure 12) (Cardoso *et al.*, 2003; France *et al.*, 2009; Monaco, 2017; Assef, 2023; Rafael *et al.*, 2024).

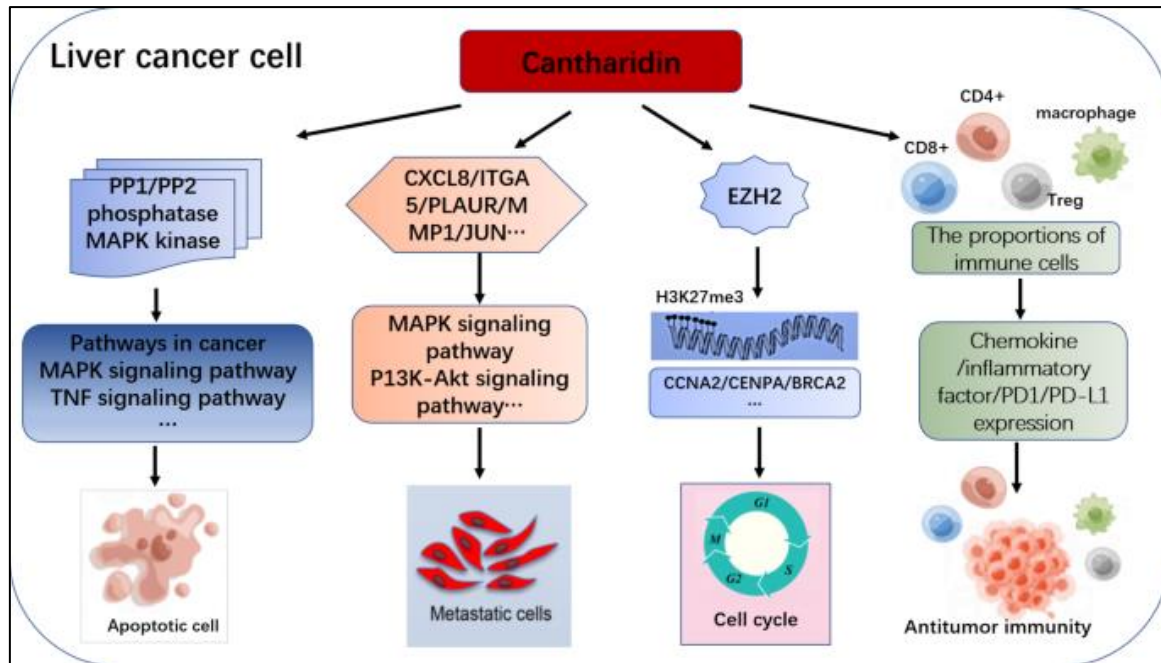


Figure 12: Figure The function of cantharidin in HCC. Cantharidin is involved in regulation the of cell apoptosis, EMT progresses, EZH2/H3K27me3 related cell cycle pathway, and immune response to exerting antitumor function in HCC

Source: <https://doi.org/10.1186/s12906-023-03975-0>

“Cantharidin is known to have an irritating effect and is sometimes used to remove epithelial warts or remove tattoos in humans. However, in the Middle Ages, this compound was obtained from certain beetles such as *L. vesicatoria* and sold as an aphrodisiac, as it stimulated erections when consumed orally, however, this practice has presented a high risk due to its high toxicity in humans”, Coleoptera venom can inhibit the proliferation of tumor and non-tumor cells through the secretions of the pygidial gland (Ibáñez) (Cardoso *et al.*, 2003; Franceet *al.*, 2009; Monaco, 2017; Assef, 2023; Rafael *et al.*, 2024).

8. CONCLUSION

The medical importance linked to these beetles is because they have a terpene in their hemolymph insect blood that is soluble in various organic solvents, but practically insoluble in water, cantharidin. Only synthesized male cantharidin is stored until mating and transferred to the female at the time of copulation. When molested, these insects expel the toxin through the membranous joints of the body, causing vesicles similar to burns on human skin. Meloid beetles generate a poisonous chemical compound to, among other things, defend themselves from their predators. An international research team involving the Complutense University of Madrid has shown that cantharidin is toxic to several common parasites. The results explain that some birds, such as the great bustard, ingest this type of beetle, among other beneficial properties, due to the antiparasitic activity of cantharidin.

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