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# Composition of ant venom (Hymenoptera: Formicidae) presenting real therapies and possibilities

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## 1. Introduction

Ants are invertebrate animals, with the largest number of species in the insect group. They belong to the Phylum Arthropoda, Order Hymenoptera, and all species are part of the Family Formicidae. There are approximately 18,000 species of ants. In Brazil, there are around 2,000 species, making it the country with the greatest diversity of ants in the Americas [1-3].

In general, the size of ants can vary between 0.2 centimeters and 2.5 centimeters. Additionally, most of these insects are black, brown, or red, but may have a metallic sheen and green tint. Anatomically, ants have three pairs of legs, a pair of compound eyes, a pair of antennae, and a pair of mandibles. The pair of jaws make up your chewing mouthparts, essential for your lifestyle habits. Metapleural glands that secrete an antibiotic fluid. As for food, it can be said that it varies depending on the species. Leafcutter ants, for example, feed on fungi that they grow in their anthills. Meanwhile, other species use plant sap, nectar, insect shells, and human food remains for their food. In moments when they feel threatened, the ant's bite releases a type of chemical known as formic acid, which can Leave. cause pain, itching, or swelling (Figure 1) [1-4].

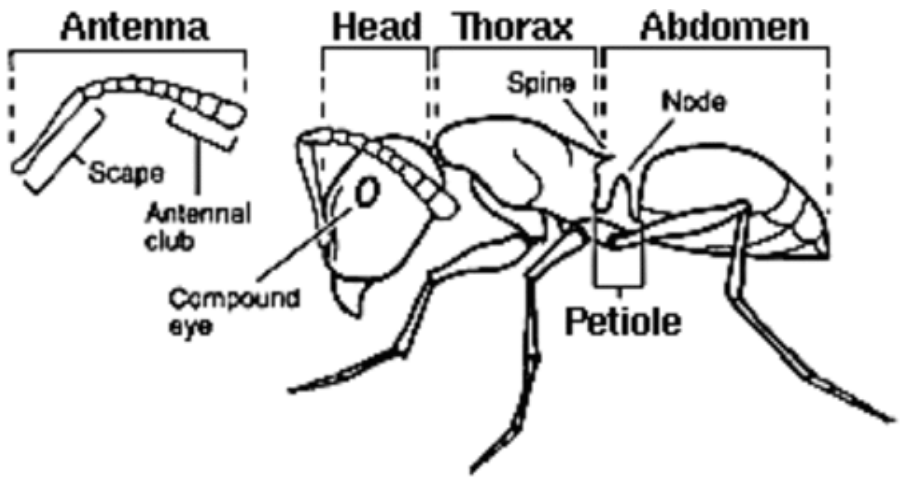

**Figure 1.** Ant morphology. Source: https://extension.umn.edu/insects-infest-homes/ants.

Although they do not directly transmit diseases, some dangers lurk in these animals, as they travel through places such as landfills and sewers and feed on dead insects, such as cockroaches. When they feed on these animals and pass through these areas, they carry with them parasites, bacteria, microbes, and fungi that are very harmful to our health. Ants have a cosmopolitan distribution. They are found on all continents. Ants occupy a wide range of ecological niches and exploit diverse food resources as herbivores, predators, and direct or indirect scavengers. Most ant species are generalist omnivores, but some are specialized in feeding [4-8].

An exoskeleton is an outer covering that provides a protective shell around the body and an attachment point for muscles, in contrast to the internal skeletons of humans and other vertebrates they have a long, thin, perforated tube along the top of the body called the dorsal aorta, which works like a heart and pumps hemolymph towards the head, thus boosting the circulation of internal fluids. The nervous system consists of a ventral nerve cord that runs the length of the body, with numerous ganglia and branches along the way (Figure 2) [9-12].

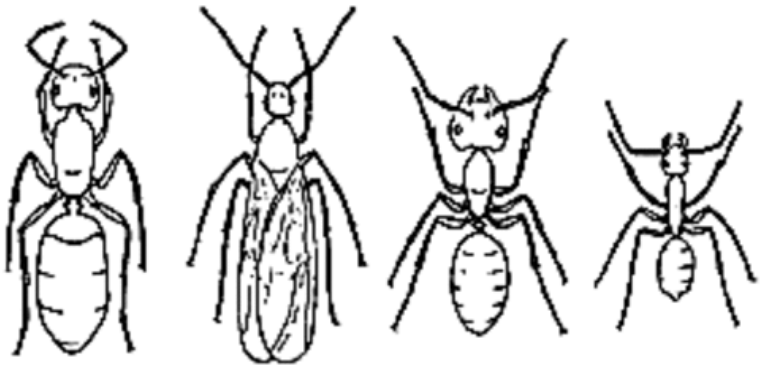

**Figure 2.** Typical ant castes, from left to right: queen, winged male, major worker, minor worker. Sources: https://extension.umn.edu/insects-infest-homes/ants#ant-castes-41460 and the University of Minnesota.

The functions they perform in the environment and their food sources depend on the species. Some can assist in seed dispersal and germination, soil aeration, and predation by other invertebrates. Some species of ants are considered pests, especially those that occur in human homes, where their presence is often problematic. Some species of ants are considered pests, especially those that occur in human homes, where their presence is often problematic. Some ants attack stored food, some seek out water sources, some may damage interior structures, some may damage crops directly or by aiding sucking pests, and some sting. Ant populations are managed by a combination of approaches using chemical, biological, and physical methods [12-15].

Ant eggs are small, oval, white, translucent, and only 1 mm long and 0.5 mm in diameter. The only exception is the larger eggs from which a new queen will emerge. After seven to fourteen days, when the eggs hatch and turn into larvae. They are also translucent, worm-like creatures without eyes or legs. Pupae start white, have a waxy exterior, and eventually darken (Figure 3) [16-18].


**Figure 3**. Egg, larva, and pupae of the ant *Pseudomyrmex gracilis* (Fabricius, 1804) (Hymenoptera: Formicida) Metamorphosis & Ant Brood. Source: Alex Wild Photography

The pupae of some species create a cocoon as a form of defense, while others are exposed or naked and may eventually darken. The pupae of some species create a cocoon as a form of defense, while others are exposed or naked. It can take 6 to 10 weeks from the time the queen lays her eggs to the point the ant is fully grown. After the colony matures, at a certain time of the year, some larvae are fed a diet rich in proteins to become future queens. In addition, the queen's mother also begins laying unfertilized eggs to become future males. Nuptial flight: when adverse conditions change, the young queens and males leave the anthills en masse and gather in a nuptial flight where they mate. After mating, the queens lose their wings and start new colonies, while the males die after a short time (Figure 4) [18-20].

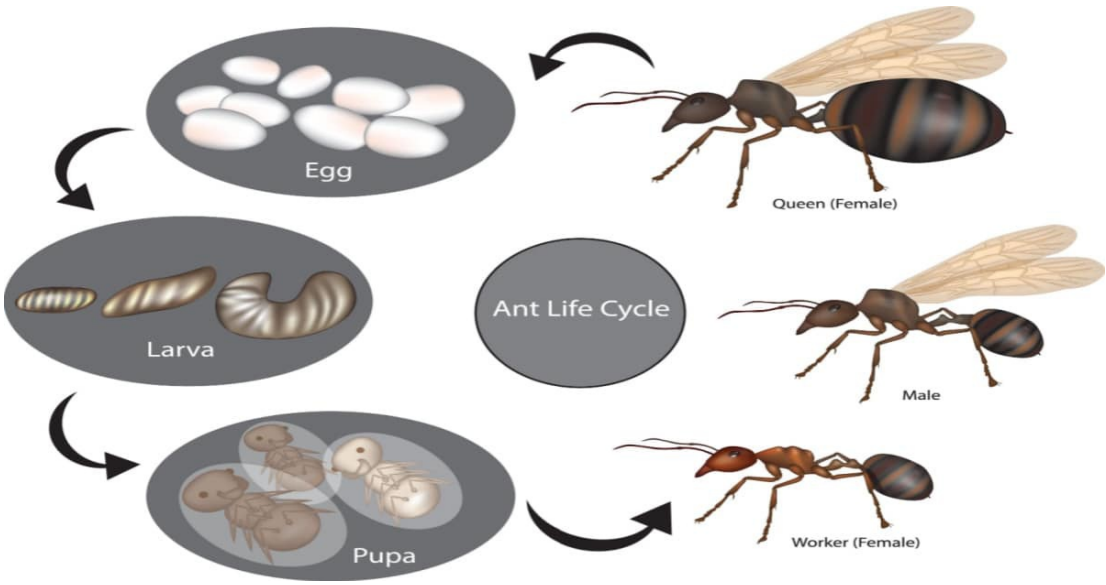


**Figure 4.** Ant life cycle. Source: By Nato Lagidze. Source: https://www.learnaboutnature.com/insects/ants/ant-life-cycle/.

In general, they are organized into three castes: The Queens who live from 10 to 20 years and are responsible for the continuity of the species, as they are the only ones who can reproduce. An anthill does not necessarily have a queen, the number varies according to the species. The males have a short life span, ranging from a week to years, they have no function in the anthill and only serve to mate with the queen and die. Workers are the females that are in greater quantity in the colony, they take care of the anthill and also take care of the queen and her offspring [19-22].

**2. Some Groups of Ants**

A. Fire ants, this insect has a color that varies from yellow to dark brown. They are omnivores and are attracted to meat and oil. These ants usually build their nests on the ground or inside trees. When threatened, they moderate and inject a poison whose sting is quite painful and, in some cases, can even cause allergies (Figure 5) [20-22].

**Figure 5.** Fire ant sting pustules formed on the side of man's hand. Sources: Photo by Bart Dress and https://ant-pests.extension.org/fire-ant-stings/.

B. Carpenter ants, also called termites, get their name because their nests are usually built in wooden environments, but they do not feed on this material. They prefer sweet foods but can also eat meat and eggs.

C. Leafcutter ants have a color that varies from yellowish brown to black. They build their nests in the ground and feed mainly on a fungus extracted from plants that lead to the anthill. This group is made up of several species, the best known of which are sauvas.

D. Pharaoh ants also known as sugar ants; This species has a yellowish to brown color. They are omnivores and feed mainly on fats and sweets. They are considered a risk to public health because they are vectors of bacteria that can cause infections.

E. Ghost ants are pale to dark in color on the head and mesosoma, while the feathers and gaster are yellowish. They prefer to live in humid places, which is why they are often found in kitchens and bathrooms, on top of the sink, or the floor [23-25].

**Some of the species**: *Acromyrmex* spp., *Atta* spp., *Camponotus* spp., *Monomorium* spp., *Paratrechina* spp., *Pheidole* spp., *Solenopsis* spp. and *Tapinoma melanocephalum* (Fabricius. 1793) (Figure 6) [24-25].

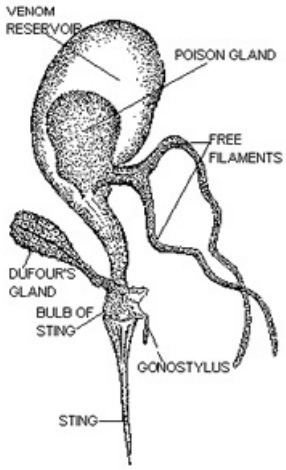


**Figure 6.** Poison gland – A poison gland containing venom is attached to the stinger. Queen and winged reproductive (unmated queen) ants also have a poison gland. However, they do not use their ovipositors as stingers, as do worker ants.

### 3. Poison composition and therapeutic possibilities and real therapeutic

Ants, like other animals, get sick. In some cases, they combat the problem with substances with an antibiotic effect that they produce themselves. A study carried out by researchers at the University of North Carolina, in the United States, shows that these natural remedies are so powerful that they have the potential for use in humans. Details of the work were recently published in the journal Royal Society Open Science. 20 species of ants exposed to the bacteria *Staphylococcus epidermidis* (Evans 1916) (Bacillales: Staphylococcaceae) were studied so that researchers could evaluate **the antibiotic effect of the insects'** reaction. The species that produced the most powerful substance was *Solenopsis molesta* (Say 1836), a tiny ant common in the United States and Canada (Figure 7) [25-30].

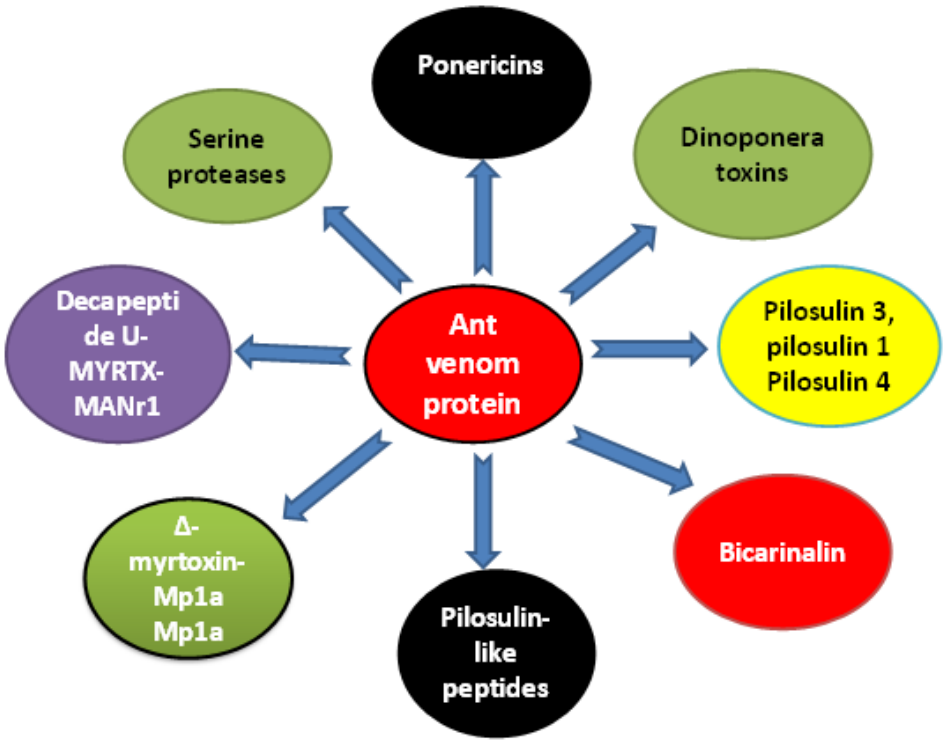


**Figure 7.** Venom – The venom of imported fire ants is produced in the poison gland. It contains two major components: alkaloids and proteins. The oily aliphatic alkaloids (i.e., the piperidine alkaloid, Solenopsin A) are toxic to cells. Piperidine is a relative of piperine, the main chemical ingredient in black pepper. Source: Fire Ant Project Fact Sheet, Medical Problems and Treatment Considerations for Red Imported Fire Ant Stings.

The data suggests that some ant species are capable of producing potent and promising compounds for the development of a new medicine. The compound was tested against *S. epidermidis*, a common microbe on human skin. Therefore, it is possible that **the antimicrobial action of ants (natural antibiotics)** can kill pathogens that infect humans, according to one of the study's authors. The scientist emphasizes that much more testing is needed to reach clinical use of the substance (Clint Penick researcher at the University of Arizona). They provide us with guidance for searching for promising compounds in ants (Márcia Renata Mortari - University of Brasília) (Figure 8) [26-30].

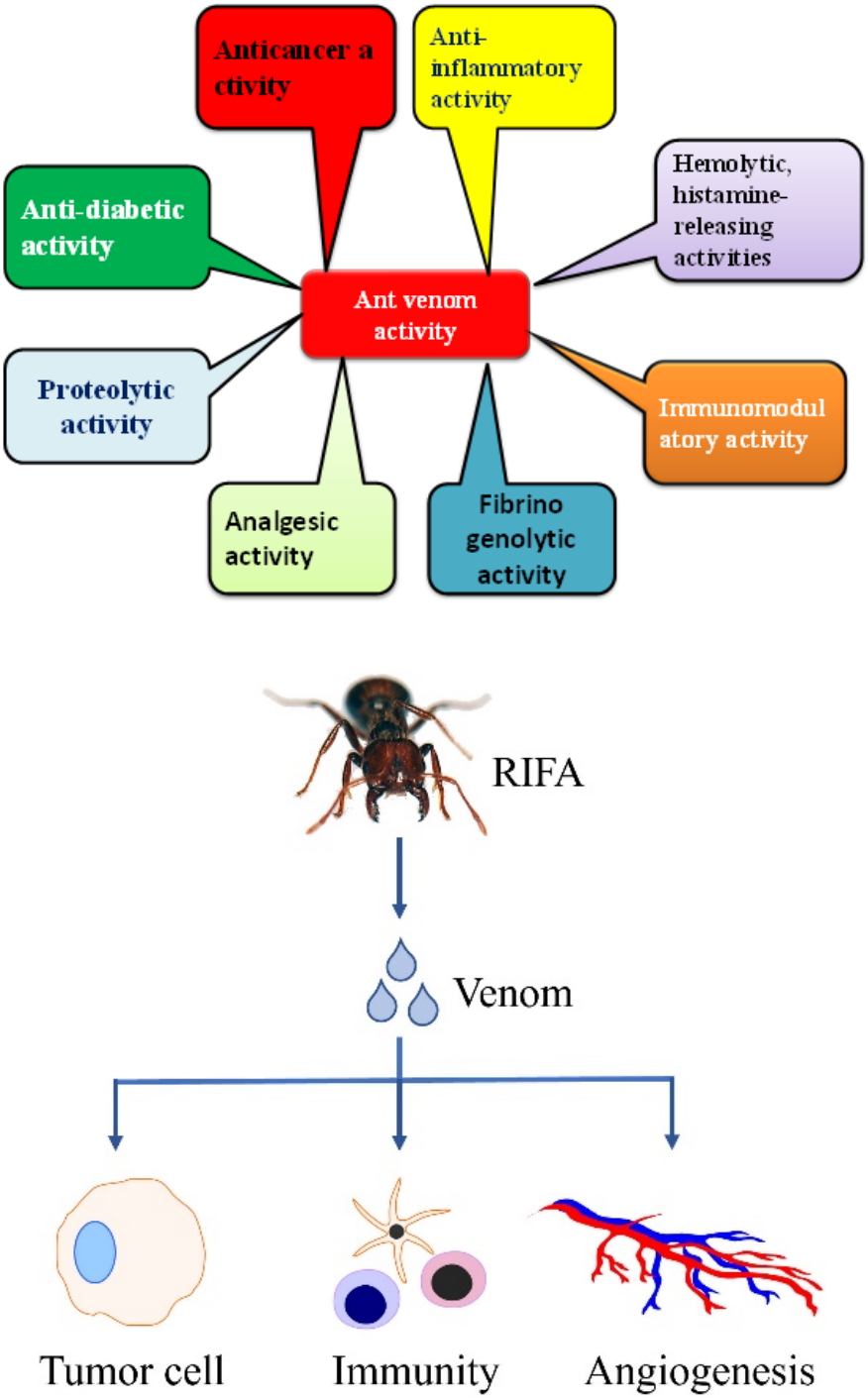


**Figure 8.** Showing different effects of ant venom toxins and Therapeutic use of the venom secreted by red imported fire ants (RIFA) has a potential anti-tumor effect. Source: Front. Immunol., 21 May 2023, Section Cancer Immunity and Immunotherapy, Volume 14 - 2023 | https://doi.org/10.3389/fimmu.2023.1200659.

In addition to determining that all four three-dimensional forms of the alkaloid exist in the venom of *S. saevissima,* the researcher also discovered that the mixing ratio of the different forms varies, within the same anthill, according to the size of the insect. **The poison has fungicidal or bactericidal effects** on the eggs, and the poison must play an important role in identifying caste and species, he said. The venom's alkaloids and cuticular hydrocarbons are very abundant and can be spread throughout the environment [Eduardo Fox, from the Federal University of Rio de Janeiro]. The work focused on

standardizing the methodology for analyzing 2-methyl-6-undecylpiperidine in the venom of S. saevissima, but there are also other alkaloids in the venom of this species – as well as that of other *Solenopsis* species [28-32].

Some people around the world experience pain and skin irritation**resulting from psoriasis, a chronic disease**. Scientists have discovered that a compound derived from fire ant venom can eliminate this incurable autoimmune disease, giving hope for new treatments. The new research, led by a team from Emory University in the United States, and published in the journal “Scientific Reports”, revealed that solenopsin, the main toxic component of this insect's venom, carries a powerful compound similar to ceramide, which helps protect the skin. Solenopsin, the main toxic component of the venom of these fire ant ants, bears a strong chemical similarity to molecules called ceramides, which help protect the skin [29-33].

Ceramide maintains the skin barrier by helping the epidermis repel microorganisms, which is why they are used in a wide variety of skin medications. But there's a problem with ceramide: in some circumstances, the molecule can degrade into sphingosine-1-phosphate (S1P), a compound that can cause inflammation. Having observed the molecular similarities between solenopsin and ceramide. He and his team developed two analogous venom samples that looked like ceramide but could not be converted to S1P  (Figure 9) [33-36].

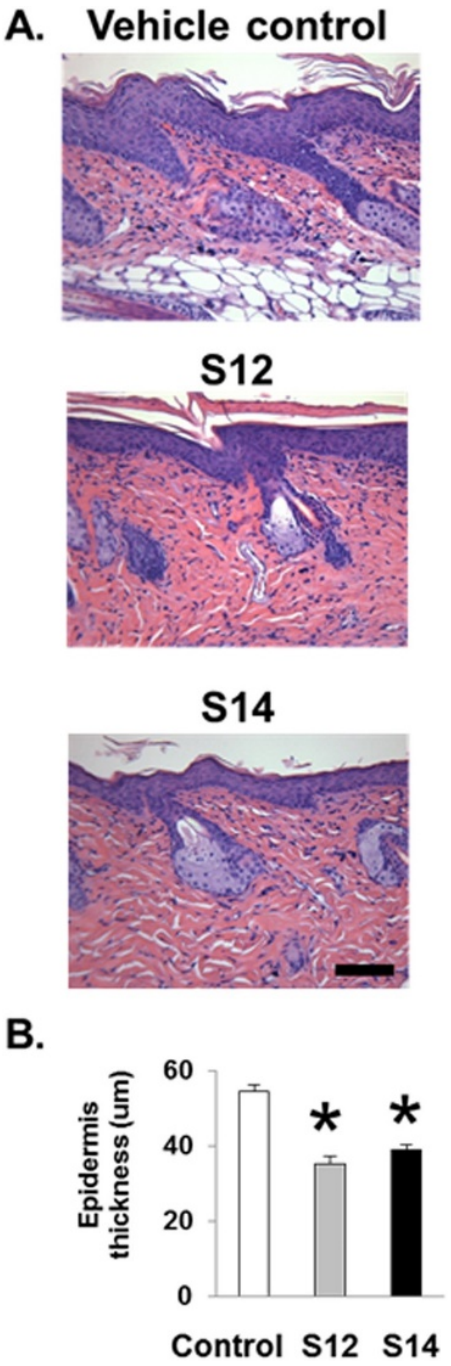


**Figure 9.** Treatment of inKC-Tie2 mice with S12 and S14 results in decreased epidermal thickness (acanthosis). (A) Representative images of H&E-stained dorsal skin sections from KC-Tie2 mice following treatment with S12, S14 or vehicle cream. (B) Quantification of epidermal thickness (μm) of H&E-stained dorsal skin sections of vehicle-treated (n = 8), S12 (n = 9) and S14 (n = 9) KC-Tie2 mice. The values shown represent the mean ± SEM. Data were analyzed using a student's t-test. P values are as indicated. Scale bar = 50 μm. Scientific Reports. 2017; 7:11198. https://doi.org/10.1038/s41598-017-10580-y.

Ceramide maintains the skin barrier by helping the**epidermis repel microorganisms**, which is why it is used in a wide variety of skin medications, including those that treat eczema. But there's a problem with ceramide: in some circumstances, the molecule can degrade into a compound that can cause inflammation. And that's where the poison of

foot wash comes into play (Figures 10-11) [36-37].

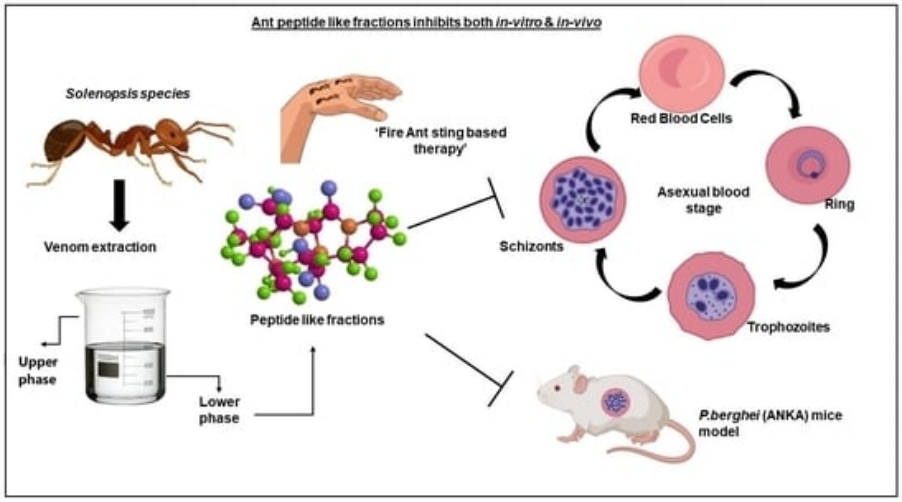


**Figure 10**. Figure Prevailing drug resistance in malaria imposes the major roadblock for the existing interventions necessitating the timely need to search for alternative therapies. Ants in *Solenopsis* spp., termed 'Fire ants', are well known for their aggressive behavior, which leads to the release of toxic venom. Notably, the tribal natives of the malaria-laden densely forested Bastar region, Chhattisgarh, India, use fire ant sting-based therapy to cure malaria-like high fever. Inspired by this, we have collected the fire ants from the forest of Bastar and extracted peptide and alkaloid fractions from ant venom using HPLC and analyzed them by LC/MS-based applications. Evaluation of the anti-malarial efficacy of these peptide fractions demonstrated a significant reduction in the growth of Plasmodium falciparum (Pf 3D7) in vitro, whereas the alkaloid fraction showed a negligible effect. In vitro, hemolytic activity confirmed the venom peptide fraction to be non-hemolitic. Source: Toxins 2022: 14(11): 789. https://doi.org/10.3390/toxins14110789.

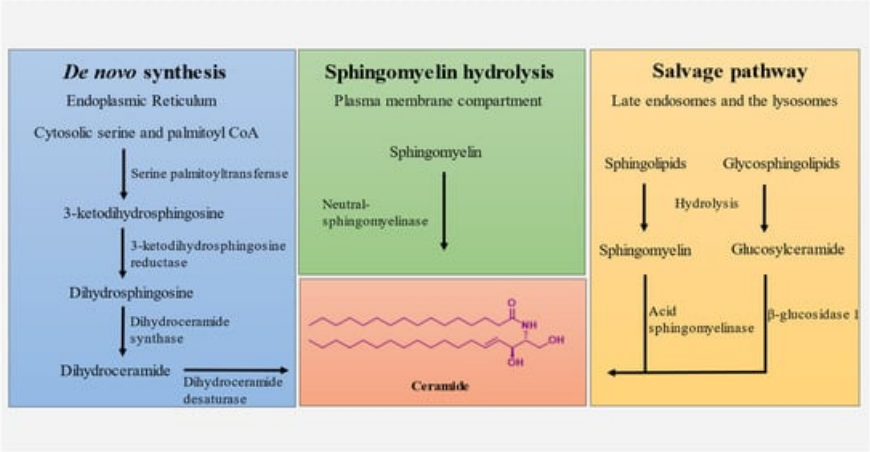


**Figure 11.** Ceramide synthesis pathways; de novo synthesis, sphingomyelin hydrolysis, and salvage pathway. synthesis of ceramide occurs at the cytosolic leaflet of the endoplasmic reticulum. The reaction is primarily initiated by the condensation of cytosolic serine and palmitoyl CoA by serine palmitoyltransferase to produce 3-ketodihydrosphingosine.

In turn, 3-ketodihydrosphingosine is reduced to dihydrosphingosine by 3-ketodihydrosphingosine reductase, followed by the production of dihydroceramide by dihydroceramide synthase. Subsequently, dihydroceramide is catalyzed by dihydroceramide desaturase to form ceramide, which is transported to the Golgi apparatus. Biomedicines 2022: 10(8): 1956. https://doi.org/10.3390/biomedicines10081956.

Observing the similarities between solenopsin and ceramide, he and his team developed two samples analogous to the venom ingredient that looked like ceramide but without the ability to convert it into an **inflammatory compound** [Jack Arbiser - Dermatologist] [37-39].

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