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Centipede venom (Arthropoda: Scolopendromorpha: Scolopendridae) with therapeutic potential.

Carlos Henrique Marchiori[1]

1 Instituto Federal Goiano

Potential competing interests: No potential competing interests to declare.

Marco Vinícios de Oliveira Santana[1], Klebert de Paula Malheiros[1]

[1]Department of Biology and Medicine of the Marco Santana Institute, Goiânia, Goiás, Brazil.

The chilopoda, popularly known as centipedes belong to the Phylum: Arthropoda Subphylum Myriapoda; Class Chilopoda, Order Scolopendromorpha; Family Scolopendridae. The centipede is a myriapod with a flat body of the head and a series of equal segments, with no distinction between the thorax and abdomen. The head has a pair of antennae, a pair of mandibles, and two pairs of mandibles. The first pair of legs, the maxillipeds, function as defensive weapons. The outer skeleton of the centipede's body is divided into numerous articulated segments, which overlap, allowing the animal to curl up. And the hind legs are bigger than the front ones (Figure 1) [1-2].

Figure 1. *Scolopendra morsitans* Linnaeus, 1758. Source: Photo 44828926, (c) Adam Brice.

No external morphological characters were observed that would reveal sexual dimorphism and differences between life stages. The variable characters are mostly related to tergite 21 and the prefemoral spine number and configuration of the last pair of legs. An integrative study between molecular data and properties of *Colopendra viridicornis* Newport, 1844 (Scolopendromorpha: Scolopendridae) venom can help elucidate the relationships between *C. viridicornis* populations, and a study of ontogenetic development can contribute to understanding life stages within the genus (Figures 2-3) [2-5].

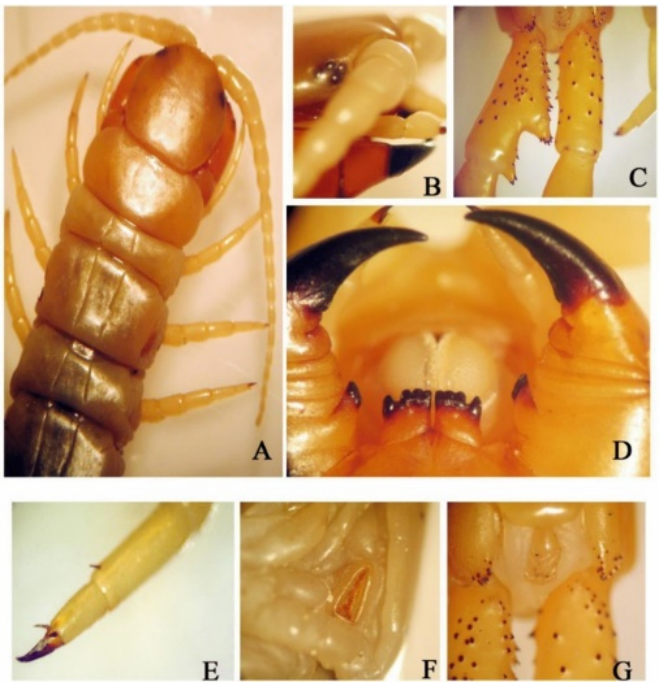

Figure 2. *Scolopendra canidens* Newport, 1844, **A** Head plate with antenna and trunk segments, **B** 4 eyes in lateral sides, **C** Prefemure of the terminal leg, **D** forcipular coxosternal teeth plate, trochant-prefemoral process, and 2 poisonous claw in the ventral side, **E** leg with 3 lateral spines, **F** spiracle, **G** prefemure of the ultimate leg with coxsoternal process with spines in ventral view. Source: https://doi.org/10.1007/s00435-022-00573-5.

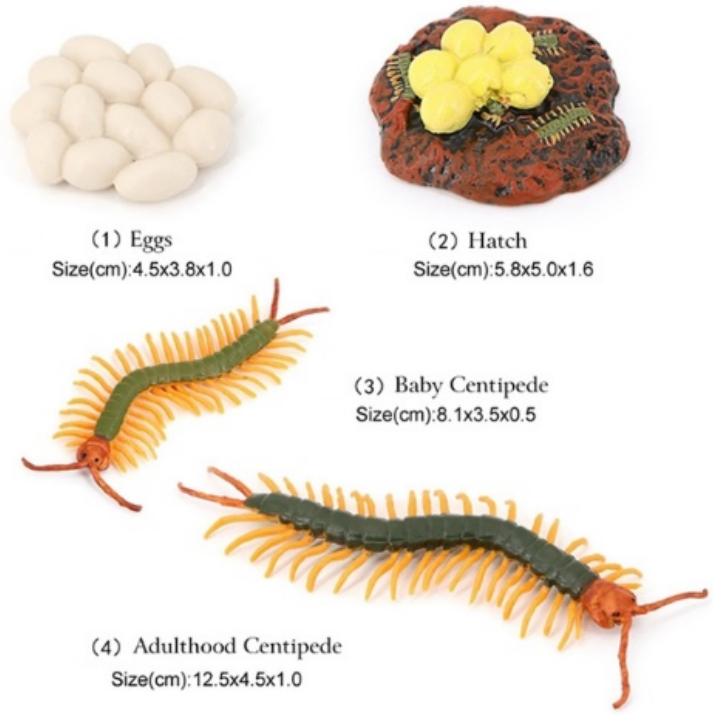

Figure 3. The life cycle of a centipede. Sources: UC Master Gardeners of Napa County weekly column and

https://ucanr.edu/blogs/napanewspaper//blogfiles/97225_original.jpg.

Also known as centipedes, they live in damp and dark places, such as holes, gardens, rocks, pots, or places with rubbish and debris. During the day they are less visible and it is more common for them to come out of their hiding places at night. They are very agile in moving and attacking prey. These animals preferentially feed on larvae, earthworms, worms, insects, rats, and baby birds [3-6].

The centipede is, in turn, prey for owls, hedgehogs, shrews and frogs. Centipedes reproduce by laying eggs, which are placed in cracks and holes in the ground, or other protected and moist places, such as under rocks, logs, or leaves. Larvae hatch from eggs and undergo several molts before reaching their adult form [3-7].

Giant centipede this centipede is a fierce predator of worms, slugs, and insects. With the help of two long antennae, the animal locates its prey, which is immobilized by a precise bite from its sharp stingers. They are not real teeth, but modified legs, capable of injecting venom into the victim. With its jaws, the centipede tears its prey apart. Common centipede the common centipede generally attacks animals of its size, including other centipedes. It has 15 pairs of legs [3-8].

They live in humid environments, under logs, rocks and leaves. Poisonous centipede some species of centipede, such as those of the *Scolopendra* Linnaeus, 1758 found in Africa, Asia, and the Americas, reach up to 30cm in length. Sometimes centipedes enter people's homes, looking for insects. The venom from their bite is lethal to these small animals in humans, it causes mild poisoning [5-9].

These animals are generally nocturnal, preferentially feeding on larvae, earthworms, worms, insects, mice, and baby birds. Centipedes are very efficient predators, to do this, they use their poisonous claws to paralyze their prey. However, they can also have a herbivorous diet, with the potential risk of causing economic losses in cases of overpopulation (Figure 4) [1-9].

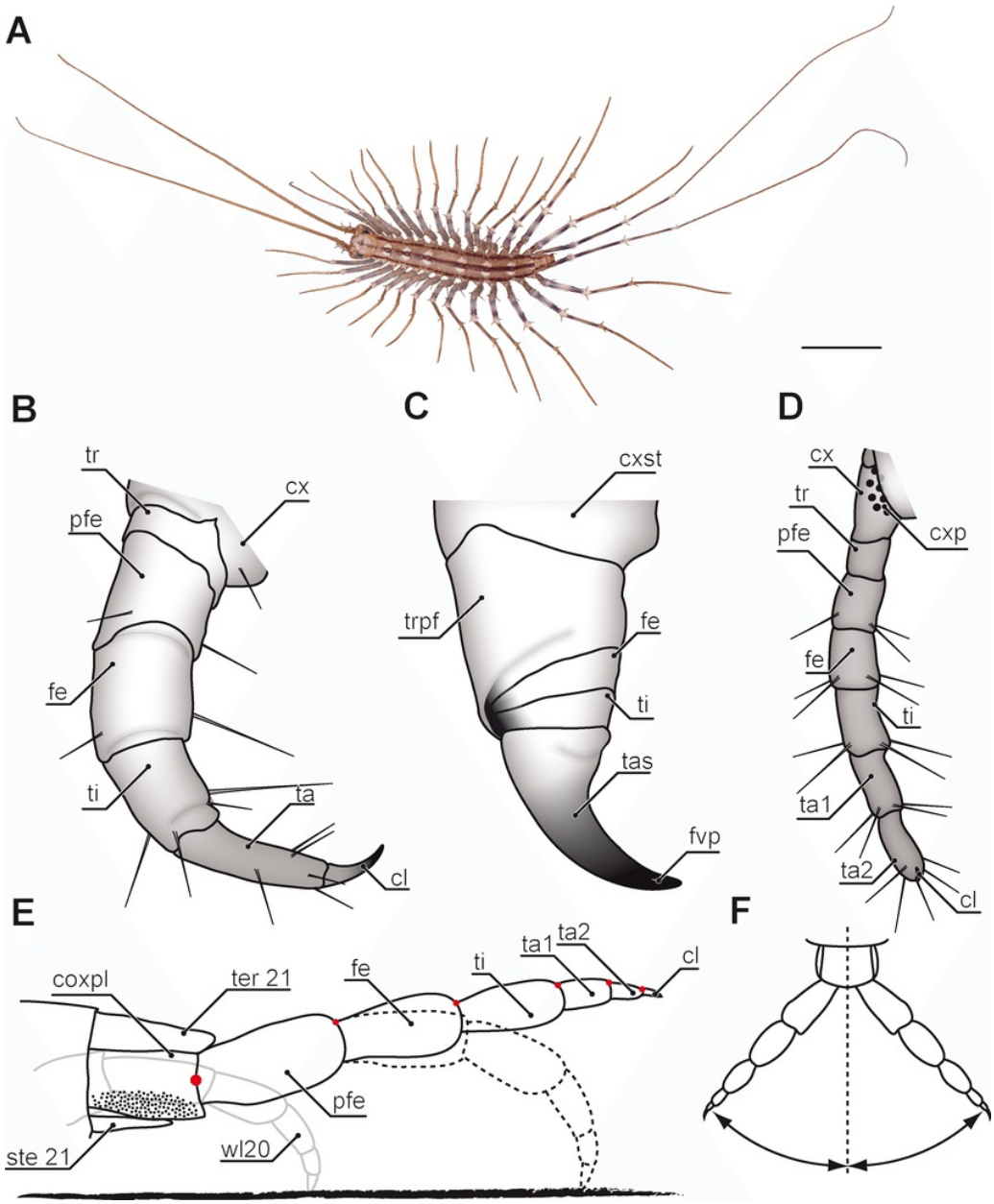

Figure 4. Overview of centipede appendages. (A) Habitus of *Scutigera coleoptrata* (Linnaeus, 1758), from dorsal. Walking legs gradually increase in length along the body axis. Note the resemblance of the anterior (left) and posterior (right) poles of the body (Original). (B-D) Schematic representations of serially homologous, modified arthropod of *Geophilus flavus* De Geer, 1778, not to scale. (B) Walking leg 10 (view from posterior, Original). (C) The forcipule with the typical shared joint of distal podomeres (view from ventral, modified after Haug et al., 2014). (D) The ultimate leg with thigh pores (view from ventral, Original). (E) Articulation and movement of ultimate legs in *Scolopendra morsitans* Linnaeus, 1758 (lateral view, modified after Jangi, 1961). Elevated leg (solid line), resting leg (dotted line), and walking leg 20 for size comparison (solid gray line). Dorsoventral movements are restricted by dorsally located pivot joints (red dots). (F) Horizontal movements are restricted by the joint between coxopleura and prefemur (compare E, modified after Jangi, 1961). Scale bar: A 1 cm. Abbreviations: cl, pretarsal claw; cx, thigh: cxp, coxal pores; cxpl, coxopleura; cxst, coxosternitis; fe, femur; fvp, forcipular venom pore; pfe, prefemur; ste21, sternum 21; ta, tarsus; ta1, tarsus 1; ta2, tarsus

2; tas, tarsungulum; ter21, tergite 21; ti, tibia; tr, trochanter; trpf, trochanteroprefemur; wl20, walking leg 20. Full-size. Source: DOI: 10.7717/peerj.4023/fig-1.

Underneath the head, they have a pair of forcipules poisonous stingers that function as pincers capable of injecting venom. The last pair of legs is not used for locomotion, but rather as a sensory organ and for capturing food. The venom is largely composed of metalloproteases and has neurotoxic, cardiotoxic, and myotoxic activity. Centipedes are not known vectors of infectious diseases and do not carry pathogenic microorganisms. However, due to their aggressive nature and the possible introduction of bacteria through their fangs, a secondary infection can occur at the bite site if left unattended (Figure 5) [10-14].

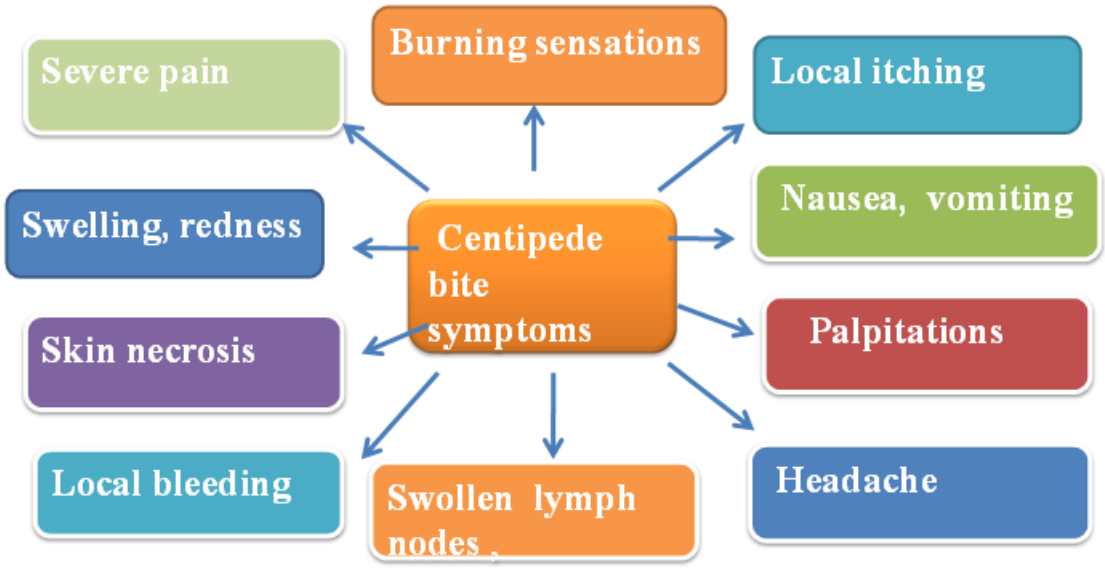

Figure 5. Symptoms of centipede bite. Source: © 2022 The Authors. Published by Innovare Academic Sciences Pvt Ltd. DOI: https://dx.doi.org/10.22159/ijpps.2022v14i9.45488. Journal homepage: https://innovareacademics.in/journals/index.php/ijpps.

In a comparative study of the venom glands of Brazilian centipedes*S. viridicornis*, *Cryptops iheringi* Brölemann, 1902 and *Otostigmus* Porat, 1876, great morphological similarity was demonstrated, except concerning the size of the glands, which was proportional to the body size of each species studied Studies carried out by Australian, Chinese, and Mexican researchers have identified that the venom of some species of centipedes, *Scolopendra subspinipes mutilans* Koch, 1878, and other myriapods can be used to relieve intense pain, whether chronic or not. The experiments are carried out by extracting venom from the animals' jaws, which, if they come into direct contact with humans, can cause pain, swelling, and even skin rashes (Figure 6) [10-14].

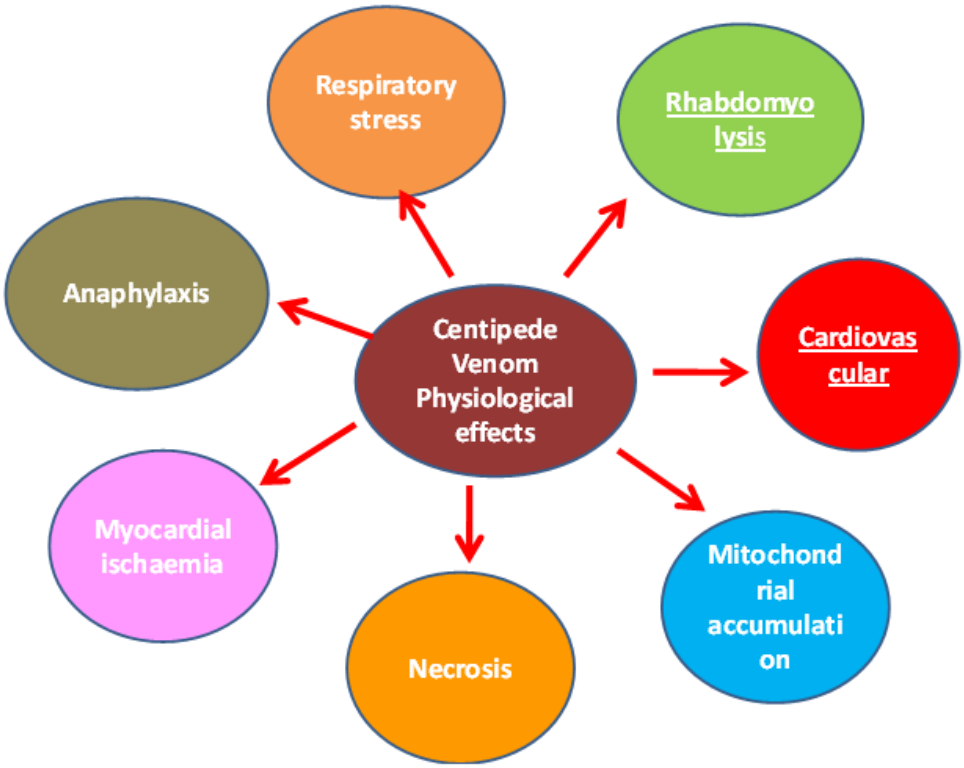

Figure 6. Physiological effects of centipede venom. Source: © 2022 The Authors. Published by Innovare Academic Sciences Pvt Ltd. (https://creativecommons.org/licenses/by/4.0/). DOI: https://dx.doi.org/10.22159/ijpps.2022v14i9.45488. Journal homepage: https://innovareacademics.in/journals/index.php/ijpps.

However, when processed in the laboratory, the venom can inhibit pain. Humans have a protein called "Nav1.7" responsible for transmitting pain throughout the body. When analyzing this substance, scientists realized that the venom can affect this protein and in some cases, it can inhibit it up to 150 times more than morphine and other conventional pain relief medications. However, not all cases were in which the poison had the same inhibition capacity as morphine. The big issue is that the poison does not cause drug addiction, because it does not block receptors, unlike morphine (Figure 7) [10-14].

The NaV1. 7 human is one of the 9 functional isoforms of voltage-gated sodium channels, they are transmembrane proteins, mainly expressed in cells of the peripheral nervous system, being closely related to the perception and transmission of pain [10-14].

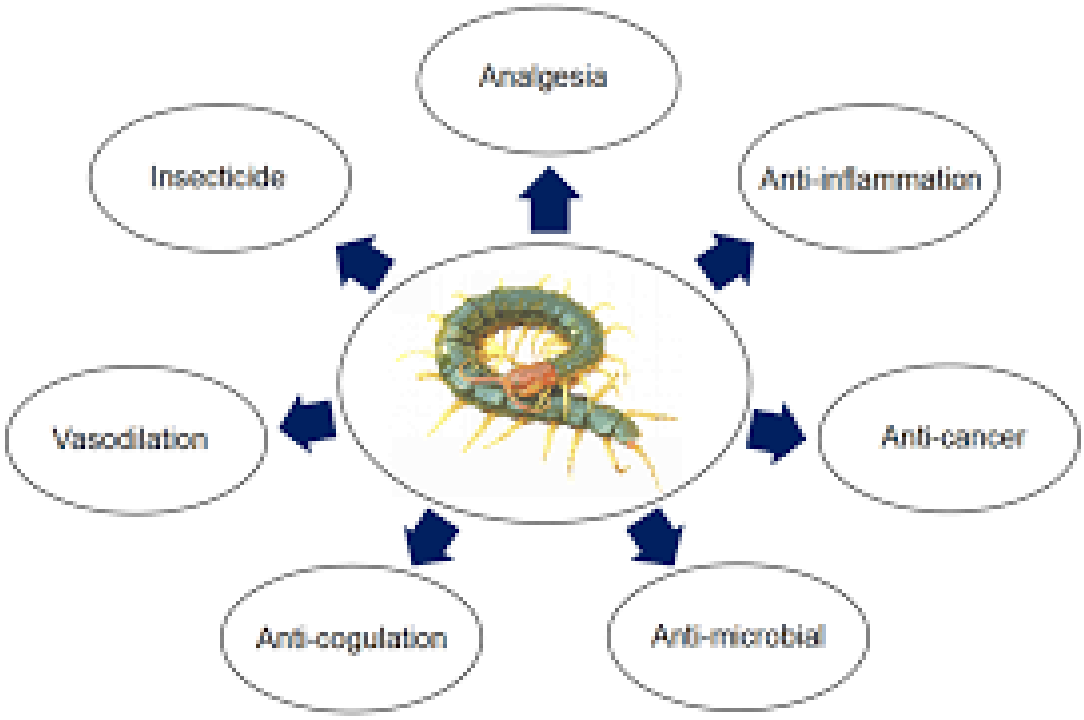

Figure 7. Functions of bioactive peptides and proteins from centipede. Source: doi.org/10.3390/molecules27144423.

In addition to recent research into the potential of centipede venom, several substances from venomous animals have been used for medicinal purposes. In addition to the inoculation of snake venom to alleviate the effects of bites, blue scorpion venom, when processed in laboratories, can be applied as an alternative treatment for patients with various types of cancer (Figure 7 [10-14].

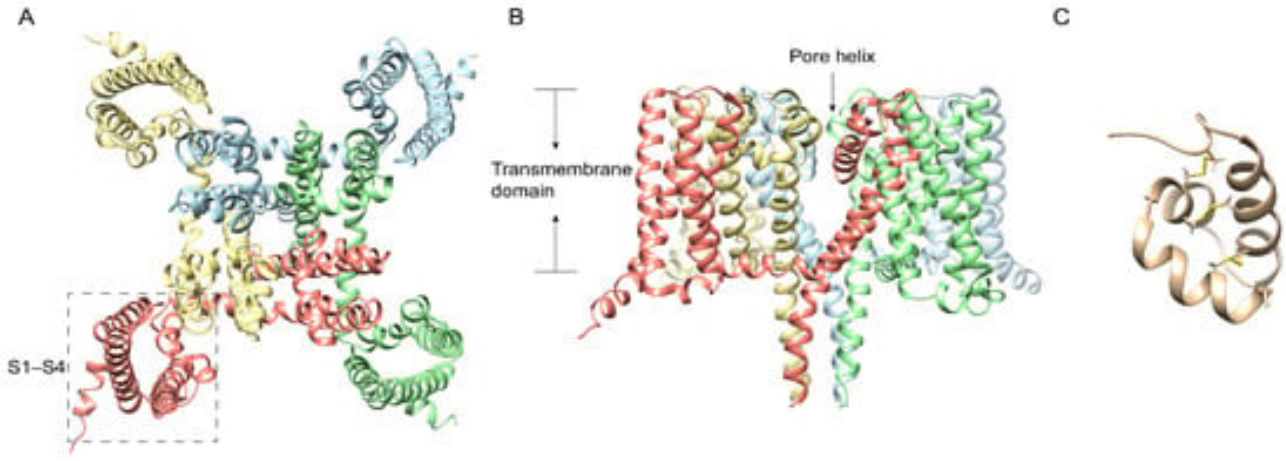

Figure 7. Ribbon diagram of human NaV1.7 atomic model (PDB id: 5EK0) with each of the four subunits color-coded, showing views from the bottom (A) and side (B). The voltage-sensing domain is labeled with a dashed box. The membrane-spanning helices and different subunits of the NaV1.7 channel are indicated. (C): μ-SLPTX-Ssm6a from the Chinese red-headed centipede Scolopendra subspinipes Bücherl, 1946. PDB id: 2MUN. Source: Int. J. Mol. Sci. 2022,

23(13), 7105; https://doi.org/10.3390/ijms23137105.

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