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Public Health Impact and Potential Biomedical Applications of Solenopsis Invicta Venom

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ADMINISTRATIVE INFORMATION

Support - No support.

Review Stage at time of this submission - Data extraction.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 September 2024 and was last updated on 23 September 2024.

INTRODUCTION

Review question / Objective This scoping review aims to summarise the scientific evidence on the potential therapeutic applications of Solenopsis invicta venom in medicine, assessing whether its alkaloids and peptides offer genuine benefits in the treatment and prevention of human diseases.

Background Numerous species of arthropods, including Solenopsis invicta (red imported fire ant), produce venoms that contain a variety of biochemical compounds with both harmful and beneficial properties for human health. In public health, insect stings can lead to localized reactions, systemic allergic responses, anaphylaxis, and even death. Some species also transmit infectious diseases through their stings, increasing the risk of pathogen spread. However, research has shown that these venoms can also have therapeutic potential, demonstrating antimicrobial, anti-inflammatory, analgesic, and anti-tumor properties, which could lead to novel drug development.

Recent studies, particularly between 2023 and 2024, have revealed an active field of research into the biomedical applications of insect venoms. For instance, melittin from Apis mellifera and Apis florea exhibits antiviral and anti-inflammatory effects, while peptides from Vespa magnifica show potential in treating rheumatoid arthritis. Among ants, the venom of Dinoponera quadriceps contains dinoponeratoxins, which may have anticonvulsant effects for epilepsy treatment. Additionally, bicarinalin, isolated from Tetramorium bicarinatum venom, has been investigated for its efficacy against Helicobacter pylori, which is responsible for gastric diseases. Peptides from Paraponera clavata show analgesic effects, and Polyrhachis lamellidens venom, studied for its anti-inflammatory properties, is a potential therapeutic agent for Alzheimer's disease.

The venom of Solenopsis invicta has been extensively studied, particularly for its antitumor and antimicrobial activities. Solenopsis invicta

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belongs to the Formicidae family and lives in colonies that range from 80,000 to 400,000 individuals, establishing nests identified as soil mounds. Native to South America, this species has spread globally, creating ecological, agricultural, and health-related concerns due to its aggressive behavior and venomous stings. The venom contains alkaloids and peptides that cause intense pain, inflammation, and in some cases, anaphylaxis. These venom components, particularly solenopsins, have drawn interest for their pharmacological potential.

Rationale Solenopsin A, an alkaloid found in Solenopsis invicta venom, has been shown to inhibit angiogenesis and block the PI3K-Akt pathway, which plays a role in cancer growth and metastasis. Its antiangiogenic properties are significant in the treatment of neoplasms, as it interrupts cancer cell survival by preventing new blood vessel formation. Solenopsin A is also reported to mimic ceramide, a lipid that regulates cell death and proliferation, making it a potential agent in treating hyperproliferative conditions such as psoriasis. These findings suggest that solenopsin and its analogues could be used as therapeutic agents in oncology and dermatology.
Despite the promise of Solenopsis invicta venom in treating bacterial infections, protozoa-related diseases (like Leishmaniasis and Chagas disease), and cancer, its potential remains largely unproven in human clinical trials. Current evidence is limited to in vitro studies and animal models. The venom has shown inhibitory effects on biofilm formation by bacteria, as well as antifungal activity against Candida albicans and Cryptococcus neoformans. Studies have also demonstrated its efficacy against drug-resistant strains of bacteria, including methicillin-resistant Staphylococcus aureus (MRSA).
In conclusion, Solenopsis invicta venom presents exciting possibilities for medical application, particularly in inhibiting microbial biofilms, treating fungal infections, controlling protozoa, and targeting cancer growth. However, more comprehensive research, particularly human clinical trials, is required to substantiate these preliminary findings and explore its full therapeutic potential.

METHODS

Strategy of data synthesis The data set to be extracted was defined in advance by the authors and included: the main author, publication date, study location, type of study (microbiological, in vivo or cell line), the specific disease analyzed, the active ingredient of the Solenopsis invicta venom used and the main results. The extracted data were entered into Word tables by the two reviewers independently and subsequently compared to check for concordance. The final results are presented in tables.

Eligibility criteria All studies involving Solenopsis invicta venom in the context of treatment and prevention of human diseases were considered potentially eligible. No restrictions were imposed on publication year or language, as long as an abstract was available in English. Inclusion criteria included clinical and preclinical studies (in vitro and in vivo) investigating therapeutic effects and potential medical applications, such as antibacterial, antitumor and anti-inflammatory activity. Exclusion criteria included studies with weak or unclear methodological design, studies not peer-reviewed or published in sources of questionable reliability, duplicate studies or studies with redundant information already present in other publications. Literature reviews were excluded, but used as sources of literature search and for information purposes.

Source of evidence screening and selection The research was conducted using three databases (PubMed, Scopus, and Science Direct) and one registry (Cochrane Library), with an additional search in grey literature through Google Scholar and OpenGray (DANS EASY Archive). It is important to note that textbooks were identified and retrieved along with other records (reports, articles, studies, doctoral theses, proceedings) using databases such as ScienceDirect and Google Scholar, which index them, alongside PubMed and Scopus to a certain extent. Relevant articles were also searched from references in literature reviews on Solenopsis invicta.
The search process took place between September 1, 2023, and October 10, 2023, with a final update of records on July 1, 2024. Subsequently, on March 3, 2024, an additional literature search was conducted using other databases such as EBSCO, Web of Science, and LILACS. The authors (M.D.) used specific keywords, including Solenopsis Invicta, RIFA, Hymenoptera, Formicidae, fire ant, and solenopsin. The selection of potentially eligible studies was performed by two reviewers (M.D. and D.S.), with a third reviewer (A.B.) assigned to resolve any conflicts in inclusion decisions. The eligibility criteria, databases, and keywords were jointly determined by the reviewers, who then independently conducted the searches, reporting the number of records retrieved for each keyword and database. Duplicate records from different databases were removed using EndNote 9

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software, and if necessary, manually during the screening process. Both screening and study inclusion were conducted independently, with a subsequent comparison of the results between the two reviewers.

Data management The data were summarized and reported in tables, and subjected to verification by further reviewers in order to minimize reporting errors.

Language restriction No language restrictions were imposed on the search.

Country(ies) involved Italy.

Keywords Solenopsis invicta; RIFA; Tumor; Psoriasis; Antimicrobial; Trypanosoma; Angiogenesis; Venom; Leishmania; Candida.

Contributions of each author

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