Research Square

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Bibliometric Analysis of Spider Venom Research Based on ITGInsight

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Abstract

Spider venom garnered significant attention in the medical field due to its diverse biological activities, as well as its complex chemical constituents and promising pharmacological values. Based on 845 publications indexed in the Web of Science Core Collection from 2014 to 2025, a bibliometric analysis was conducted using ITGInsight software to systematically examine the global research landscape in this domain. The findings revealed that an overall increasing trend was observed. Brazil (221 publications), China (144 publications) and the United States (141 publications) were identified as the leading contributing countries, with the U.S. playing a central role in international collaboration networks. The journals *Toxins* (108 articles, 1,645 citations) and *Toxicon* (76 articles, 950 citations) were recognized as core outlets in the field, while research focus was observed shifting from early efforts in venom component identification toward exploring molecular mechanisms and medical applications. Beyond the bibliometric analysis, this study provides a comprehensive analysis of the chemical constituents and pharmacological values of spider venom, highlighting their potential applications in drug development and biomedicine. It also offers an overview of the current research landscape, serving as a valuable reference for future investigations.

1. Introduction

Spiders (Araneae) are among the most diverse orders of arthropods, comprising over 50,000 described species distributed across a wide range of ecosystems worldwide(Edwards and Powell 2025, Zamani 2025). In recent years, increasing attention has been directed to their venom systems, owing to the complex biochemical composition and diverse biological functions characteristic of spider venom(Lüddecke, Herzig et al. 2022, Guo, Guo et al. 2024). Spider venom, a complex biological fluid secreted during predation and defense(Dresler, Avella et al. 2024), contains a rich repertoire of bioactive molecules, including neurotoxins, cytotoxins, and various enzymatic components (Benli 2013). Many of these compounds exhibit remarkable specificity for ion channels and receptors, making spider venom a valuable natural resource for drug discovery and biomedical applications.

The chemical diversity and pharmacological potential of spider venom have been extensively documented. Neurotoxins represent one of the most characteristic components, with many families of spider-derived toxins demonstrating high-affinity modulation of voltage-gated sodium and calcium channels(Pringos, Vignes et al. 2011, Agwa, Tran et al. 2020). In addition to neurotoxins, spider venom contains cytolytic peptides and small-molecule compounds that collectively constitute its complex chemical arsenal(Windley, Herzig et al. 2012, Kuhn-Nentwig 2021, Pereira, Cavalcante et al. 2023). In terms of bioactivity, accumulating evidence has revealed the therapeutic potential of spider venom components, including multi-target regulation of ion channels implicated in neuropathic pain, as well as selective cytotoxicity against various cancer cell line(Wu, Wang et al. 2019). These findings underscore the promise of spider venom as a source of lead compounds for novel therapeutic development.

In recent years, advances in high-throughput sequencing and mass spectrometry have enabled the transition of spider venom research from traditional component identification toward the exploration of molecular mechanisms and clinical applications. For instance, integrated transcriptomic and proteomic analyses were effectively used to map the toxin diversity of Macrothele bannaensis, revealing a complex cocktail of bioactive peptides(Zheng, Yin et al. 2025). Furthermore, ecological adaptation studies reveals evolutionary diversification in venom composition(Pekár, Bocánek et al. 2018), with venom complexity associated with predatory strategies and geographic variation observed across populations(Langenegger, Nentwig et al. 2019, Lyons, Dugon et al. 2025).

As an analytical methodology integrating statistics, data mining and visualization, bibliometrics is employed to systematically examine academic output, collaborative networks and research hotspots within specific domains(Kokol, Vosner et al. 2021). Its application has expanded in the biomedical field(He, Liu et al. 2025), where it and demonstrates considerable utility in both tracking emerging research trends and evaluating scholarly impact in recent years. For instance, a recent bibliometric study on marine microphytoenthetic biofilms successfully employed network visualization to map research clusters and identify key thematic areas(Finnerty, Galán-Pérez et al. 2025).

ITGInsight is an advanced bibliometric analysis platform that leverages text mining and network visualization to uncover hidden relationships within large-scale literature data(Wang, Zhang et al. 2022). Its application in academic research has expanded across diverse domains including ecology, health, sports, and social sciences. For example, a bibliometric study utilizing ITGInsight analyzed 4,215 propolis-related publications from the Web of Science Core Collection (2014–2024), mapping national contributions, institutional collaborations, author impacts, and thematic evolution, thus highlighting its value in systematically reviewing research landscapes and guiding future directions in natural product studies(Wang, Liu et al. 2026). These studies underscored the platform’s strong capabilities in complex technology analysis especially in integrating diverse data sources visualizing knowledge networks and supporting strategic decision-making.

Despite substantial progress in spider venom research, current investigations remain relatively fragmented and lack a systematic assessment of overarching developmental trends. This work aims to provide a systematic interpretation of the current research landscape, which will offer valuable insights for future studies and promoted further advancements in medical and other related fields.

2. Research Data Selection and Investigative Approaches

2.1 Data Sources and Literature Screening Process

Data for the present study were retrieved from the Web of Science Core Collection (WOSCC), and is recognized as one of the most reliable sources for bibliometric investigations due to its comprehensive coverage of high-quality scientific publications worldwide. A topic search strategy was employed to query the database for literature published between January 1, 2014, and June 30, 2025, using the key

term "spider venom". Furthermore, the search was restricted to documents in English and only articles and reviews were included.

The initial search yielded a total of 1291 publication records. Following the application of restrictions based on document type and language, 1179 records were retained. To ensure analytical accuracy, a rigorous manual screening protocol was implemented. First, clearly irrelevant studies were excluded based on title evaluation. Subsequently, further refinement was conducted through a comprehensive review of abstracts. These selected articles cover several prominent research directions within spider venom investigations, including venomics, molecular mechanisms of action, and pharmaceutical applications. All included documents were exported in plain text format and imported into the ITGInsight platform for further bibliometric analysis. Finally, through this multi-stage screening procedure, 812 high-quality publications were identified for inclusion. The data retrieval strategies for this study are summarized in Fig. 1.

2.2 Research Methodology

The bibliometric analysis was conducted using ITGInsight V2.5 C, with key parameters set as follows: term length was limited to 2–4 words, standardized stopword lists were employed to perform stopword filtering, and the filter_wos1_author_use_fullname_doi_as_id filter was applied to ensure data consistency. The dataset, covering the period from 2014 to 2025, was refined based on a Top N (N = 30) selection criterion.

3. Results

3.1 Analysis of Published Research Articles

As shown in Fig. 2, the annual number of peer-reviewed publications on spider venom research from 2014 to 2025 follows a dynamically stable trend. After an initial drop from 71 papers in 2014 to 54 in 2015, the field rebounded steadily, with annual output fluctuating between 58 and 82 papers from 2016 onward. Publications peaked at 82 in 2022, then declined year-on-year to 75 (2023), 69 (2024), and 58 (2025). Across the full period, annual output hovers near 70 papers in most years, confirming sustained scholarly interest in spider venom research despite a modest recent decline.

3.2 Country Analysis

3.2.1 National Co-authorship Analysis

As evidenced in Table 1, Brazil has the highest number of publications (226), followed by China (149) and the United States (146). Australia ranks fourth with 126 publications. Publication counts decline steadily from the fifth rank onward: England (47publications), Germany (39), Mexico (37), France (35), Russia (25), and Belgium (23).

International co-authorship data reveals a globally distributed collaborative network for spider venom research, with the United States serving as a core collaboration hub. As illustrated in Fig. 3, the strongest collaborative links are observed between the United States and Australia (29 joint publications), followed by the United States and Brazil (23 joint publications). Other notable collaborative partnerships include China–United States (12 joint publications), Brazil–France (12 joint publications), Germany–United States (9 joint publications), Germany–Australia (7 joint publications), and Brazil–Belgium (8 joint publications).

Table 1
Top 10 countries by number of counts

Rank	Country	Counts
1	Brazil	226
2	Peoples r china	149
3	USA	146
4	Australia	126
5	England	47
6	Germany	39
7	Mexico	37
8	France	35
9	Russia	25
10	Belgium	23

3.2.2 Cross-national Publication Analysis

As listed in Fig. 4, Brazil's academic output in venom research is particularly prominent, with its publication counts in *Toxins* (30 articles) and *Toxicon* (28 articles) significantly exceeding those of other countries. Concurrently, Brazil's leading output in the *Journal of Venomous Animals and Toxins Including Tropical Diseases* (23 articles) further emphasizes its deep engagement within this specialized subfield. China's research contributions are primarily concentrated in *Toxins* (26 articles) and *Toxicon* (14 articles), while substantial research capability is also demonstrated through its output in *Comparative Biochemistry and Physiology D-Genomics & Proteomics* (7 articles), which reflects China's active exploration in spider venom genomics and proteomics. The United States exhibits a broader distribution of research outputs, with notable contributions observed in *Scientific Reports* (5 articles) and the *Journal of Biological Chemistry* (3 articles), evidencing its leading role in interdisciplinary spider venom research. Australia's efforts are mainly channeled through *Frontiers in Pharmacology* (6 articles) and *Neuropharmacology* (7 articles) and highlight its distinctive contributions to pharmacological mechanism studies of spider venom.

3.3 Journal Analysis

As a vital channel for disseminating research findings, academic journals play a crucial role in reflecting scholarly quality. A detailed analysis of the top 10 journals in the field of spider venom research is conducted to assess its academic influence. As presented in Table 2, the top 10 journals in the field of spider venom research are listed. *Toxins* has the highest number of publications (111) and citations (1,646). *Toxicon* follows with 82 publications and 951 citations. The *Journal of Venomous Animals and Toxins Including Tropical Diseases* ranks third with 37 publications and 350 citations. Other journals include *Frontiers in Pharmacology*, *International Journal of Biological Macromolecules*, *Plos One*, *Scientific Reports*, *International Journal of Molecular Sciences*, *Biochemical Pharmacology*, and *Toxicon-X*. Summarily, the top ten journals suggest that spider venom research focuses on chemical constituents and its bioactivities and mechanism.

Meanwhile, a trend toward diversification in platforms disseminating spider venom research is illustrated through analysis of journal evolution mapping. As depicted in Fig. 5, the prominence of *Toxins* is interpreted to underscore its central role as a core outlet in toxinology and indicates sustained academic interest in spider venom. Initially concentrated in specialized toxinology journals, early research later expands to include journals such as *Fronti ers in Pharmacology*, effectively extending the scope of inquiry into pharmacological applications.

Table 2
Top 10 journals by number of publications

Rank	Journal	Publications	Count of citations
1	Toxins	111	1646
2	Toxicon	82	951
3	Journal Of Venomous Animals And Toxins Including Tropical Diseases	37	350
4	Frontiers In Pharmacology	20	450
5	International Journal Of Biological Macromolecules	18	135
6	Plos One	15	244
7	Scientific Reports	14	302
8	International Journal Of Molecular Sciences	12	68
9	Biochemical Pharmacology	12	213
10	Toxicon-X	12	77

3.4 Institution Analysis

The analysis of institutional affiliations (Table 3) reveals that the University of Queensland in Australia (100 publications) is the most productive institution, followed by Hunan Normal University in China (76 publications) and the Federal University of Minas Gerais in Brazil (63 publications). Other notable contributors include the University of São Paulo, the National Autonomous University of Mexico, and Masaryk University. Notably, four institutions from Brazil are ranked in the top 10, while Australia and China also exhibit considerable academic influence in spider venom research.

Analysis of the institutional collaboration network (Fig. 6) indicates that the University of Queensland serves as a central hub in spider venom research, with core focuses on spider venom (29 publications), ion channels (19 publications), and voltage-gated sodium channels (19 publications), maintaining extensive partnerships with institutions across the global research network. Among other leading nodes, Hunan Normal University is the most prominent Chinese institution in the network, with a strong research focus on with a strong research focus on spider venom (23 publications), peptide toxins (15 publications), and ion channels (10 publications), and exhibits notable collaborative influence in the field. Brazil's Universidade Federal De Minas Gerais is another key international hub, with its research centered on spider venom (11 publications), loxosceles venom (10 publications), and synthetic peptides (10 publications), forming close collaborative ties within the network. Other active institutions in the collaboration network include Masaryk University Brno, Dali University and the Pushchino Scientific Center of the Russian Academy of Sciences, which together form the core global collaborative clusters in this research field.

Brazil's leading position in spider venom research is consistently reflected across national, journal, and institutional levels. As the top-ranking country in publication output (226 publications), Brazil also dominates the core venom-specific journals, including *Toxins, Toxicon*, and t*he Journal of Venomous Animals* and *Toxins Including Tropical Diseases.* This strong journal presence is further supported by the fact that four Brazilian institutions—the Federal University of Minas Gerais, the University of São Paulo, the Butantan Institute, and the Federal University of Paraná—rank among the top ten most productive institutions worldwide. Together, these findings underscore Brazil's comprehensive and sustained leadership in the field of spider venom research.

Table 3
The top 10 institutions in spider venom research

Rank	Institution	Country	Publications
1	University Of Queensland	Australia	100
2	Hunan Normal University	Peoples R China	76
3	Univ Fed Minas Gerais	Brazil	63
4	Univ Sao Paulo	Brazil	26
5	Univ Nacl Autonoma Mexico	Mexico	24
6	Masaryk Univ	Czech Republic	22
7	Russian Acad Sci	Russian	21
8	Butantan Inst	Brazil	21
9	Univ Fed Parana	Brazil	21
10	Univ Sunshine Coast	Australia	18

3.5 Co-authorship Analysis

An analysis of author collaboration patterns serves to identify core scholars and their cooperative relationships within a research domain. As displayed in Fig. 7, Glenn F. King is the most pivotal scholar in spider venom research, with core research focuses on spider venom (14 publications), voltage-gated sodium channels (11 publications), and ion channels (7 publications). His extensive academic network forms the largest and most interconnected cluster in the field, with key collaborators including Christina I. Schroeder, Jennifer R. Deus, and Maria Elena De Lima, whose work centers on modifier toxins, chronic pain, and synthetic peptides respectively. Zhonghua Liu stands out as the leading Chinese scholar in the network, with 13 publications on spider venom, 11 on peptide toxins, and 6 on ion channels, maintaining a prominent collaborative profile with Xi Zhou. The Brazilian research cluster forms another tightly integrated group, led by Silvio Sanches Veiga and Luiza Helena Gremski, whose work focuses on brown spider and loxosceles venom, alongside key collaborator Evanguedes Kalapothakis. This closely connected team exemplifies Brazil’s consolidated expertise and collaborative research approach in the field of spider venom.

3.6 Top ten Article Analysis

Based on a co-citation analysis performed using the ITGInsight platform, the core literature network in spider venom research was identified. As shown in Table 4, the ten most frequently cited publications consisted of original research articles and reviews papers, which can be classified into four mainstream research directions in this field: #1 drug discovery and translational prospects, molecular mechanism

and #2 structural basis of spider toxins, #3 evolutionary research combined with omics technology, and #4 species-specific venom toxicology and molecular mechanism exploration.

#1 drug discovery and translational prospects, molecular mechanism. The third highly cited work was "From Animal Poisons and Venoms to Medicines: Achievements, Challenges and Perspectives in Drug Discovery" with 202 citations. This review summarized the pharmacological potential of animal venoms, including spider toxins, and discussed the challenges and prospects of translating venom-derived molecules into therapeutic drugs, highlighting the value of spider toxins as promising natural resources for novel drug development(Bordon, Cologna et al. 2020).

#2 Molecular Mechanism, Structural Basis and Pharmacological Action of Toxins. This category gathers representative studies concerning ion channel regulation, structural stability and intracellular delivery function of spider venom peptides.

The most cited paper was "Cytosolic antibody delivery by lipid-sensitive endosomolytic peptide" with 293 citations. This study demonstrated that an endosomolytic peptide derived from spider venom peptide M-lycotoxin could effectively promote the cytosolic delivery of antibodies and other proteins by disrupting endosomal membranes and inducing micropinocytosis(Akishiba, Takeuchi et al. 2017). Another influential study was "GsMTx4: Mechanism of Inhibiting Mechanosensitive Ion Channels" with 181 citations, which clarified the regulatory mechanism of spider venom peptides on ion channels through lipid membrane interaction(Gnanasambandam, Ghatak et al. 2017). The article "Potent neuroprotection after stroke afforded by a double-knot spider-venom peptide that inhibits acid-sensing ion channel 1a" received 164 citations. This study identified the spider venom peptide Hi1a as a potent inhibitor of ASIC1a channels and demonstrated its significant neuroprotective effects in experimental models of ischemic stroke models(Chassagnon, McCarthy et al. 2017). The paper "Pharmacological characterisation of the highly NaV1.7 selective spider venom peptide Pn3a" accumulated 107 citations, providing an important pharmacological basis for pain-targeted research(Deuis, Dekan et al. 2017).

The ninth-ranked article “The Cystine Knot Is Responsible for the Exceptional Stability of the Insecticidal Spider Toxin ω-Hexatoxin-Hv1a” with 93 citations revealed that the inhibitor cystine knot structural motif endows spider venom peptides with remarkable thermal, chemical and enzymatic stability, uncovering the intrinsic structural basis for the biochemical properties of spider toxins(Herzig and King 2015).

#3 Evolutionary Research and Omics Technology Application. The second-ranked article "Spider genomes provide insight into composition and evolution of venom and silk" with 220 citations. This research revealed the genomic architecture underlying spider venom and silk production and showed that venom genes evolved mainly through sequential gene duplication events (Sanggaard, Bechsgaard et al. 2014). Another notable work, "The Rise and Fall of an Evolutionary Innovation: Contrasting Strategies of Venom Evolution in Ancient and Young Animals" with 114 citations, analyzed the evolutionary dynamics of venom systems and proposed a theoretical model to interpret diversification and selection processes in venom evolution (Sunagar and Moran 2015). The tenth-ranked review “Spider Venom: Components, Modes of Action, and Novel Strategies in Transcriptomic and Proteomic Analyses” gained

92 citations. It comprehensively summarized spider venom components such as antimicrobial peptides and neurotoxins, and emphasized the increasing application of transcriptomic and proteomic strategies in venom composition analysis and novel toxin mining(Langenegger, Nentwig et al. 2019).

#4 Species-Specific Venom and Toxin Molecular Mechanisms. The review "Recent advances in the understanding of brown spider venoms: From the biology of spiders to the molecular mechanisms of toxins" received 103 citations. It summarized the composition, toxicological mechanisms and clinical effects of brown spider venom, especially focusing on the functional roles of phospholipases D and cystine-knot peptides in toxic reactions(Gremski, Trevisan-Silva et al. 2014).

Table 4
Top 10 most cited articles by total

Rank	Name	Citations
1	Cytosolic antibody delivery by lipid-sensitive endosomolytic peptide	293
2	Spider genomes provide insight into composition and evolution of venom and silk	220
3	From Animal Poisons and Venoms to Medicines: Achievements, Challenges and Perspectives in Drug Discovery	202
4	GsMTx4: Mechanism of Inhibiting Mechanosensitive Ion Channels	181
5	Potent neuroprotection after stroke afforded by a double-knot spider-venom peptide that inhibits acid-sensing ion channel 1a	164
6	The Rise and Fall of an Evolutionary Innovation: Contrasting Strategies of Venom Evolution in Ancient and Young Animals	114
7	Pharmacological characterisation of the highly NaV1.7 selective spider venom peptide Pn3a	107
8	Recent advances in the understanding of brown spider venoms: From the biology of spiders to the molecular mechanisms of toxins	103
9	The Cystine Knot Is Responsible for the Exceptional Stability of the Insecticidal Spider Toxin ω-Hexatoxin-Hv1a	93
10	Spider Venom: Components, Modes of Action, and Novel Strategies in Transcriptomic and Proteomic Analyses	92

3.7 Keyword Analysis

The ten most frequent keywords are listed in Table 5. Among them, “venom” (n = 119), “spider venom” (n = 86), and “spider” (n = 63) were identified as the most frequently occurring terms. Other commonly used keywords included “Loxosceles” (n = 41), “toxin” (n = 36), “spider toxin” (n = 31), “transcriptome” (n = 28), “brown spider” (n = 26), “spiders” (n = 25), and “toxins” (n = 25). Based on their thematic relevance, these keywords can be broadly categorized into four major research themes: (1) Core research objects and active substances: including spider, spiders, venom, spider venom, toxin, spider toxin, and toxins, which

form the foundational vocabulary of this research field. (2) Species-specific research hotspots: represented by Loxosceles and brown spider, reflecting the prominent research focus on brown recluse spider biology and toxicology. (3) Key technical approaches: highlighted by transcriptome, indicating that transcriptomic sequencing has become a mainstream method for exploring spider venom composition and evolution.

Table 5
Top 10 most keywords

Rank	Keywords	Counts
1	Venom	119
2	Spider Venom	86
3	Spider	63
4	Loxosceles	41
5	Toxin	36
6	Spider Toxin	31
7	Transcriptome	28
8	Brown Spider	26
9	Spiders	25
10	Toxins	25

3.7.1 Keyword Co-occurrence Analysis

A co-occurrence analysis of keywords can reveal the strength of associations among core research topics by quantifying the frequency of keyword co-occurrence to evaluate the distribution and developmental trends of research hotspots. As illustrated in Fig. 8, the most prominent terms identified in the network included "Venom", "Spider", "Spider Venom" and "Loxosceles". Specifically, the fundamental framework of domain research was formed by the co-occurrence of "Venom" and "Spider" 28 times. While co-occurrences were exhibited by "Loxosceles" with "Venom" and "Brown Spider" 18 and 12 times respectively, and it was also frequently associated with "Loxoscelism" and "Dermonecrosis". Meanwhile, "Toxin" and "Venom" co-occur 16 times, and "Spider Toxin" showed strong linkage with terms such as "Voltage-Gated Sodium Channel" and "Ion Channel". Furthermore, the co-occurrence of "Antimicrobial Peptides" and "Analgesic" with venom-related terms.

3.7.2 Keyword Burst Analysis

Keyword bursts, which reflected the frequent occurrence of specific terms within some time periods, could be utilized not only to reveal dynamic shifts in research hotspots within spider venom studies but

also to forecast future trajectories by tracking emerging trends. As shown in Fig. 9, the term "Venom" exhibits a sustained burst from 2014 to 2025. Burst activity for "Bioinformatics" is observed between 2015 and 2019, while "Phoneutria Nigriventer" maintained continuous burst intensity from 2016 to 2024. "Peptide" enters a burst phase beginning in 2017 and extending through 2024. A burst of "Inflammation" emerges in 2018 and persists through 2025, followed by the emergence of "LD50" in 2019, with its burst activity continuing to 2025. "Recombinant Expression" experiences a brief burst during 2020–2021, followed by the emergence of "Immunomodulation" in 2021. A single-year burst for the term "3" is detected in 2022. More recently, burst signals are detected for "Multidrug-Resistant Pseudomonas Aeruginosa" in 2023, "Androgen Receptor" in 2024, and "Plasma Membrane" in 2025.

4. Discussion

4.1. General Information

Based on a bibliometric analysis utilizing the ITGInsight tool, this study systematically examines the core characteristics and developmental trajectory of global spider venom research, encompassing annual publication trends, national and institutional collaboration networks, core journal distributions and the evolution of keyword hotspots.

Annual publication output serves as a critical indicator for assessing disciplinary growth dynamics. The annual number of publications on spider venom research remained relatively stable from 2014 to 2024, with the exception of a noticeable dip in 2015. The publication output decreased from 71 papers in 2014 to 54 in 2015, followed by a prompt recovery in subsequent years. From 2016 onward, annual output fluctuated within a narrow range of approximately 69–77 publications, indicating a generally steady level of research activity rather than pronounced growth or decline. A moderate increase was observed between 2021 and 2022, when the number of publications reached a peak of 82, representing the highest output during the study period. After 2022, publication counts showed a slight decline, decreasing to 75 in 2023 and 69 in 2024; however, these values remained comparable to those reported in earlier years and fall within the range of normal annual variation. Data for 2025 (35 publications as of June 30) are incomplete and therefore not directly comparable with full-year data from previous years. Overall, the temporal distribution suggests that spider venom research has entered a relatively mature and stable phase, with year-to-year fluctuations reflecting routine variations in publication output rather than substantial changes in research intensity or scholarly interest.

4.2 Country Distribution

Global research activity is characterized by pronounced geographical disparities and a multi-centric structure. Brazil led the top 10 countries in spider venom research with 226 publications, accounting for 27.8% and indicating its prominent role in this field. China followed with 149 articles (18.4%), while the United States ranked third with 146 publications (18.0%), closely trailed by Australia with 126 papers (15.5%). A marked decline in output is observed from the fifth position onward: England (47 publications, 5.8%), Germany (39, 4.8%), Mexico (37, 4.6%), France (35, 4.3%), Russia (25, 3.1%), and Belgium (23,

2.8%). This distribution reflects distinct regional research priorities. The strongest collaborations were identified between the U.S. and Brazil (23 co-authored papers) and between the U.S. and Australia (29 papers). Although Brazil leads in total publication volume, the United States exhibits greater international engagement and integrative capacity, reflecting a broader global academic influence. European nations such as Germany demonstrated strong research coordination capabilities through frequent collaborations with the United States and Australia (7–9 publications). While China had established a foundational cooperative relationship with the United States (12 papers), its overall international collaboration network still required further expansion. Notably, Brazil's partnerships with France (12 publications) and Belgium (8 publications) highlight substantive research ties between South America and Europe.

4.3 Journal Distribution

Journal distribution and evolution analyses elucidate the academic ecosystem of spider venom research. *Toxins* was observed to be the leading journal journals with 111 publications and 1,646 citations, demonstrating its dominant position in venom studies. It was closely followed by *Toxicon*, which recorded 82 publications and 951 citations, reflecting strong academic recognition within toxin research. The *Journal of Venomous Animals and Toxins Including Tropical Diseases* (37 publications, 350 citations) maintained its relevance through consistent performance, underscoring its specialized focus on venoms and tropical diseases. Furthermore, the higher citation rates of articles in *Frontiers in Pharmacology* (20 articles, 450 citations) and *Plos One* (15 articles, 244 citations) attest to the academic visibility and impact of the research these journals publish, highlighting its influence in pharmacological and interdisciplinary research, respectively. Meanwhile, *Scientific Reports* (14 articles, 302 citations) also demonstrated notable impact in interdisciplinary science. Although lower-ranked journals such as *Biochemical Pharmacology* were noted to have relatively fewer publications, its elevated citation count (213 citations) confirmed its specialized value in biochemical pharmacology. In summary, distinct patterns of academic engagement and influence within the spider venom research domain were revealed through the journal analysis. *Toxins* and *Toxicon* were identified to dominate in both output and citations, with *Toxins* exhibiting stronger impact through its higher citation performance. Despite their limited publication numbers, *Frontiers in Pharmacology* and *Plos One* carve out influence in pharmacology and interdisciplinary science, while *Scientific Reports* further contributes to the latter category. Meanwhile, journals such as the *Journal of Venomous Animals and Toxins Including Tropical Diseases* sustain academic relevance through specialized contributions in venom and tropical disease research. These findings highlight the diversified and complementary roles in advancing spider venom studies, which offered valuable guidance for future research dissemination. Thematically, early research was primarily devoted to venom component identification and basic toxicological analysis. With technological advances, the research focus shifted toward the functional mechanisms of bioactive venom molecules, drug development and clinical applications.

4.4 Research Hotspots and Frontiers

Keyword co-occurrence analysis reveals that "Venom," "Spider," "Spider Venom," and "Loxosceles" represent the most frequent core terms in this field. The strong co-occurrence relationship (28 times) between "Venom" and "Spider" indicated that foundational biological studies of spiders and its venoms continue to form the cornerstone of the discipline. This trend was also reflected in highly cited genomic research that investigated the evolutionary architecture of spider venom and silk genes(Sanggaard, Bechsgaard et al. 2014), which strongly corresponded to the core keywords “venom” and “spider.”

In recent years, research hotspots have significantly diversified. The terms "Toxin" and "Venom" co-occurred 16 times, and the frequent linkage of "Spider Toxin" with "Voltage-Gated Sodium Channel" and "Ion Channel" confirmed that investigations into the interactions between spider toxins and molecular targets became a central mechanistic research direction. Several highly cited studies further supported this pattern. For example, the mechanistic analysis of the spider venom peptide GsMTx4 clarified its inhibitory effect on mechanosensitive ion channels(Gnanasambandam, Ghatak et al. 2017), highlighting the importance of the keywords “spider toxin” and “toxin”. Similarly, pharmacological characterization of the NaV1.7-selective spider venom peptide Pn3a demonstrated its strong relevance to ion-channel modulation and pain research(Deuis, Dekan et al. 2017), which corresponded closely with the keywords “spider toxin” and “pain.”

Moreover, biomedical applications of spider venom peptides have increasingly attracted attention, particularly in relation to pain and neuroprotection. For instance, research identifying the peptide Hi1a as a potent inhibitor of acid-sensing ion channel 1a revealed remarkable neuroprotective effects in ischemic stroke models (Chassagnon, McCarthy et al. 2017), further emphasizing the biomedical significance of venom-derived toxins and its relationship to the keyword “pain”. Complementing these therapeutic advances, studies exploring lipid-sensitive endosomolytic peptides derived from spider venom demonstrated its ability to facilitate cytosolic antibody delivery(Akishiba, Takeuchi et al. 2017), highlighting innovative biomedical applications of “venom” and “spider venom.” Beyond direct therapeutic applications, species-specific venom research also represented an important research direction. Highly cited reviews(Gremski, Trevisan-Silva et al. 2014), summarizing the biological characteristics and toxicological mechanisms of brown spider venom further corresponded with the high-frequency keywords “Loxosceles” and “brown spider,” emphasizing the medical significance of these species in venom studies. From an evolutionary and structural perspective, two complementary lines of inquiry advanced the field. First, research exploring the evolutionary dynamics of venom systems proposed models describing diversification and selection processes in venom evolution(Sunagar and Moran 2015), reinforcing the centrality of the keyword “venom”. Meanwhile, Structural investigations of the cystine knot motif responsible for the exceptional stability of spider toxins further highlighted the biochemical properties of “toxins”(Herzig and King 2015). Finally, with the advancement of omics technologies, molecular-level analysis has become increasingly important. Comprehensive reviews of spider venom composition and analytical strategies have emphasized the growing use of transcriptomic and proteomic approaches in venom research(Langenegger, Nentwig et al. 2019), which directly corresponds to the keyword “transcriptome”. Overall, these interconnected research directions—spanning therapeutic applications, species-specific studies, evolutionary-structural biology, and omics-

driven analysis—collectively reflect the multifaceted development of spider venom research and its evolving biomedical significance.

The evolution of advanced research can be traced through keyword burst analysis, which clearly illustrates the phase-specific characteristics of disciplinary focus. Early studies were predominantly dedicated to venom component identification, as evidenced by bursts of keywords such as "Peptide" (emerged in 2017) and "LD50" (emerged in 2019). The term "LD50," a classical pharmacological metric for assessing acute toxicity and reflected the research emphasis at that stage on evaluating the safety and quantitative bioactivity of spider venoms. After 2020, the emergence of "Multidrug-Resistant Pseudomonas Aeruginosa" marked a new direction in antimicrobial research involving spider venoms. Notably, the recent bursts of "Androgen Receptor" and "Plasma Membrane" since 2023 suggested a deepening exploration of molecular mechanisms of venoms. In summary, spider venom research was observed to have evolved from an early focus on identifying core venom components toward specialized studies on particular species, active molecules such as peptides, toxicity evaluation, recombinant production techniques, medical applications including immunomodulation and antimicrobial use, and molecular mechanisms involving receptors and plasma membranes. Moreover, this progression was found to echo the broader disciplinary shift highlighted throughout this study: from traditional venom component identification toward molecular mechanism exploration and clinical translation. As noted in the Introduction and Results sections, advancements in high-throughput technologies were recognized to have facilitated this transition, enabling research to move from macroscopic descriptive studies to microscopic mechanistic investigations, and from basic toxicology toward interdisciplinary integration with pharmacology and translational medicine. Consequently, this consistent shift was regarded not only to reflect the maturation of the field but also to underscore its multifaceted developmental potential across both foundational and applied dimensions. Finally, this evolutionary trend was corroborated by shifts in journal distribution: the early dominance of specialized toxicology journals such as *Toxicon* gave way to an increasing presence of interdisciplinary journals like *Frontiers in Pharmacology* and *Scientific Reports*, indicating an expansion of the field toward pharmacological applications and cross-disciplinary integration.

Future progress could be facilitated by establishing shared databases for spider venom components and unified technical standards, which would promote global resource coordination and knowledge sharing. Subsequent research should aim to deepen venomics and mechanistic studies while prioritizing the translation of fundamental discoveries into clinical and therapeutic applications, particularly in areas such as neuroprotective treatments and anti-infective drug development to bridge the gap between basic research and practical utilization. In this context, the successful development of semaglutide, derived from the venom of the Gila monster, provides a valuable translational paradigm for venom-based drug discovery. This case illustrates how venom-derived peptides can serve as highly selective lead compounds and be transformed into clinically viable therapeutics through molecular engineering, recombinant expression, and pharmacokinetic optimization. Given the structural stability, target specificity, and functional diversity of spider venom peptides—especially those acting on ion channels,

receptors, and plasma membrane components—adopting a similar development strategy may significantly accelerate the clinical translation of spider venom-derived molecules.

4.5 Chemical constituents and Medicinal value

4.5.1 Chemical constituents

The chemical composition of spider venom primarily comprises neurotoxins, cytotoxins, enzymes, peptides and proteins, as well as small-molecule compounds. Among these, neurotoxins rapidly paralyse prey by acting on voltage-gated sodium/calcium channels and nicotinic acetylcholine receptors. For example, the neuroactive peptides of the Brazilian wandering spider modulate NaV/CaV channels (Cardoso, Walker et al. 2023), while the δ-hexatoxin and ω-hexatoxin of the funnel-web spider affect sodium/calcium channel kinetics (Cardoso, Pineda et al. 2022). Additionally, GiTx1 from the Chilean red rose spider exhibits multi-target regulation of sodium/potassium channel subtypes, demonstrating potential for the treatment of neuropathic pain(Montandon, Cassoli et al. 2020). Cytotoxins primarily cause tissue damage by disrupting the integrity of cell membranes or inducing apoptosis; for example, a toxin peptide from the Philippine bird-eating spider can induce apoptosis in MCF-7 breast cancer cells via oxidative/nitrosative stress(Lopez, Aguilar et al. 2020), whilst the cat spider-derived antimicrobial peptide GK37 inhibits Staphylococcus aureus by disrupting the cell membrane; its minimum inhibitory concentration is as low as 1.552 μM, and it exhibits low cytotoxicity towards mammalian cells(Wang, Mwangi et al. 2024). Enzymatic components (including hyaluronidases, phospholipases, proteases, etc.) primarily facilitate venom diffusion, tissue destruction and the processing of protoxins. For example, hyaluronidase and proteolytic activity have been detected in the venoms of three species of Brazilian wandering spiders, indicating their conserved nature(Fernandes, Moraes et al. 2022); Furthermore, components such as cholinesterase and phospholipase identified in the venom of monophagous spiders may contribute to other functions of the venom(Michálek, Walker et al. 2026). Peptides and proteins are the most abundant and structurally diverse components of spider venoms; they often possess inhibitory cystine-cross-link (ICK) structures, which confer high stability. A representative example is the Hc3a toxin from the Australian funnel-web spider, which modulates the inactivation kinetics of the acid-sensitive ion channel ASIC1a(Budusan, Payne et al. 2024); 98 non-redundant toxins (classified into 11 families) and 147 peptide molecules have been identified in the Chinese wolf spider(Wu, Chen et al. 2023); and the double-knot peptide Hi1a, formed by the tandem arrangement of two ICK domains, which exhibits greater pharmacological activity(Tran, Tran et al. 2021). Furthermore, although small-molecule compounds such as biogenic amines (histamine, dopamine, serotonin), polyamines and acylamines are present in low concentrations, they exert significant synergistic effects; Among these, acylpolyamines are components unique to spider venom; they inhibit ionotropic glutamate receptors and nicotinic acetylcholine receptors. Compounds of this type, represented by argiopines and Joro toxins, have become molecular templates for the design of highly effective receptor antagonists, and provide important tools for research into novel insecticides and neuroscience(Rádis-Baptista and Konno 2024).

4.3.2 Medicinal value

Spider venom is an important natural source of novel analgesic drugs, with its mechanism of action primarily involving the precise regulation of voltage-gated ion channels (such as sodium, calcium and potassium channels). For instance, the recombinant toxin rPaurTx-3 derived from the Chilean rose tarantula (Phrixotrichus auratus) effectively inhibits the Nav1.7 channel, a key target in pain signaling, with an IC_{50} as low as 25 nM, and significantly reduces the excitability of small-diameter mouse dorsal root ganglion (DRG) neurons, thereby exerting analgesic effects(Chen, Peng et al. 2020). Furthermore, the Hc3a peptide from the Australian funnel-web spider modulates ASIC1a channel activity by altering its desensitization kinetics, providing a novel strategy for the treatment of chronic pain(Budusan, Payne et al. 2024). Collectively, these studies demonstrate that spider venom peptides act on multiple pain-related ion channels and hold great promise for the development of highly efficacious and selective analgesic drugs(Souza, Binda et al. 2023).

Peptide components in spider venom exert antitumour activity through mechanisms such as the induction of oxidative stress and the regulation of ion channels. For example, peptide components from the venom of the Philippine bird-eating spider can specifically kill MCF-7 breast cancer cells via pro-oxidative and nitrosation-dependent cytotoxicity, significantly elevating intracellular levels of hydroxyl radicals, nitric oxide radicals and superoxide anions, leading to a decrease in mitochondrial membrane potential and reduced metabolic activity, and triggering typical apoptotic features such as cell membrane vesiculation, caspase activation and nuclear fragmentation (Lopez, Aguilar et al. 2020). Furthermore, these peptides can target voltage-gated sodium and calcium channels abnormally expressed on the surface of cancer cells, which play a role in tumour proliferation, migration and invasion; consequently, they hold significant value as multi-target anti-cancer lead compounds(Cardoso 2020).

Spider venom is an important source of novel antimicrobial peptides; these peptides typically possess cationic and amphiphilic structures and exert broad-spectrum activity by disrupting bacterial cell membranes. A study of the transcripome of the cat spider’s venom gland identified a novel antimicrobial peptide, GK37, which exhibits a minimum inhibitory concentration (MIC) as low as 1.552 μM against Staphylococcus aureus; its mechanism of action involves disrupting the integrity of the bacterial cell membrane. More importantly, at four times the MIC concentration, GK37 exhibits virtually no haemolytic activity and is non-toxic to human embryonic kidney cells, demonstrating excellent selectivity and making it an ideal candidate molecule for combating antibiotic resistance(Wang, Mwangi et al. 2024).

Spider venom is rich in neuroactive peptides, which can precisely regulate neural signalling by acting on voltage-gated ion channels and neurotransmitter receptors. For example, the venom of the Brazilian wandering spider contains a variety of potent sodium and calcium channel modulators, classified into four families, which significantly influence neuronal excitability(Cardoso, Walker et al. 2023); its acylpolyamides inhibit ionotropic glutamate receptors (AMPA, NMDA, KA) and nicotinic acetylcholine receptors, modulating neurotransmission at the synaptic level (Rádis-Baptista and Konno 2024). Furthermore, the compound Parawixin-11, derived from the spider Parawixia bistriata, has demonstrated significant antiepileptic effects in animal models, counteracting seizures induced by various chemical

convulsants; the mechanism may be related to the regulation of the glutamatergic system(Pereira, Cunha et al. 2025).

The active components of spider venom produce complex cardiovascular effects by modulating ion channels in cardiac muscle and vascular smooth muscle. For example, the toxin vrdg183 from the Colombian spider Pamphobetes verdolaga is a very small-molecule peptide that selectively inhibits L-type calcium channels in cardiac muscle via an allosteric mechanism, with an IC_{50} of 858.28 nM, and has no effect on potassium currents(Gómez-Restrepo, Rojas-Palomino et al. 2026). Furthermore, the venom of the Australian arboreal funnel-web spider potently modulates human Nav1.2 sodium channels and calcium channels, which is directly linked to clinical symptoms such as hypertension, tachycardia or bradycardia(Cardoso, Pineda et al. 2022). These findings not only elucidate the mechanisms of cardiovascular toxicity associated with spider bites but also provide insights for the development of novel therapeutic agents for conditions such as arrhythmia and hypertension.

4.6 Theoretical and practical implications of bibliometric analysis

The application of bibliometric analysis in this study not only systematically delineated the academic landscape and developmental trajectory of spider venom research but also provided a reference for similar studies on natural toxins. Theoretically, this work offered a comprehensive synthesis of the current state of spider venom investigations and revealed its emerging trends within the field, while simultaneously validating and extending the applicability of bibliometric methodologies through its implementation in this specialized domain.

From a practical perspective, the findings identified several key priorities of spider venom for future research, including the elucidation of targeted mechanisms of venom-derived peptides and the exploration of its potential for combating drug-resistant bacteria and developing neuroprotective applications. For research institutions and pharmaceutical enterprises, such structured analyses can be leveraged to optimize resource allocation, avoid redundant investments and accelerate the translation of bioactive venom components from basic research to clinical applications through the identification of high-impact scholars and core collaborative networks.

4.7 Implications for Policy and Decision-Making

The bibliometric analysis of spider venom literature utilizing ITGInsight offered a substantial basis for policy-making in biomedicine and ecological conservation. Research revealed spider venom's significant potential in developing analgesics that target ion channels and combating multidrug-resistant bacteria, suggesting that health authorities could prioritize funding for translational studies and enhance industry-academia-research collaboration. Meanwhile, ecological studies disclosing compositional differences between tropical and temperate venom provided scientific support for regional biodiversity strategies. Furthermore, the multipolar research landscape formed by Brazil, China, and the United States indicates that establishing international venom databases and refining cross-border cooperation could promote

equitable global resource allocation and accelerate the translation of basic research into clinical applications.

4.8 Strengths and Limitations

The present study contributes to the bibliometric analysis of spider venom research through several key innovations. First, a visual knowledge map for this field was systematically constructed using the ITGInsight platform, clearly revealing the evolution of research hotspots, collaborative networks, and development trends. Second, the dynamic evolution of the field from basic venomics towards applied research was fully illuminated through a multi-dimensional approach that synthesized analyses of national/institutional collaboration, journal distribution, and keyword co-occurrence/burst.

However, several limitations of this research should be noted. Data collection was confined to the Web of Science Core Collection, potentially excluding significant literature from other databases such as Scopus or PubMed. Meanwhile, the incomplete coverage of publications from 2026 affected the accurate interpretation of emerging research trends. Additionally, as a consequence of the reliance on standardized search queries such as "spider venom", publications employing non-standardized nomenclature remained undetected during the analysis.

5. Conclusion

A systematic analysis of the spider venom research domain was conducted through bibliometric methods and its bioactive components and medical values were summaried, which enhanced the understanding of its developmental trajectory and core research areas. By comprehensively examining spider venom's interdisciplinary progress, this study identified key research themes, understudied areas and emerging trends, offering critical insights for researchers and policymakers. The findings illustrated the multidimensional value of spider venom studies, spanning from basic science to translational medicine, while reflecting sustained academic interest in its therapeutic potential and ecological adaptations. This work not only addressed previous gaps in systematic research but also established a scientifically grounded framework for future endeavors in venom component utilization, biomedical innovation and biodiversity conservation strategies, providing significant guidance for promoting translational applications and sustainable development in this field.

Declarations

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Figures

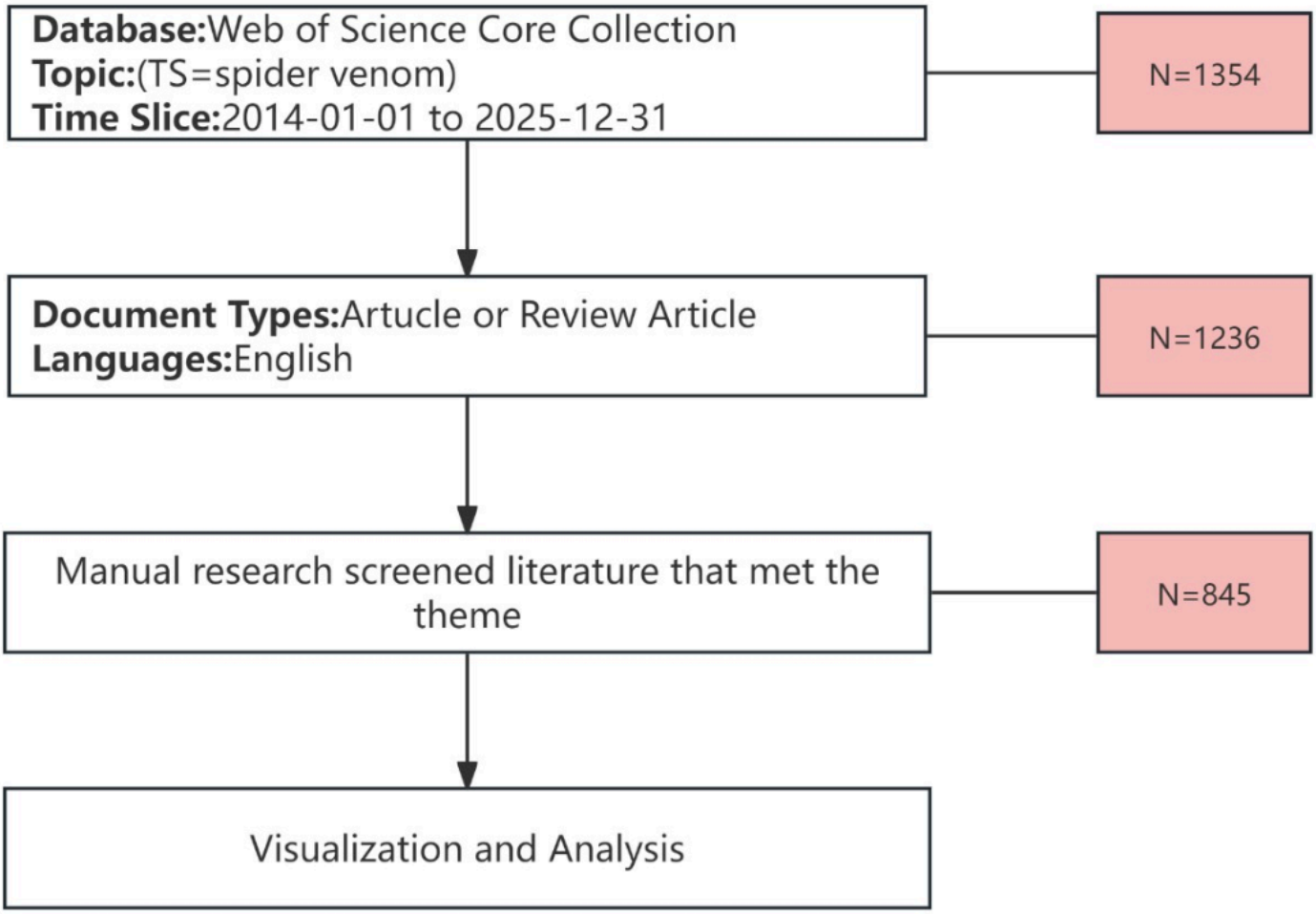


Figure 1

The literature retrieval strategy for spider venom studies employed in this research

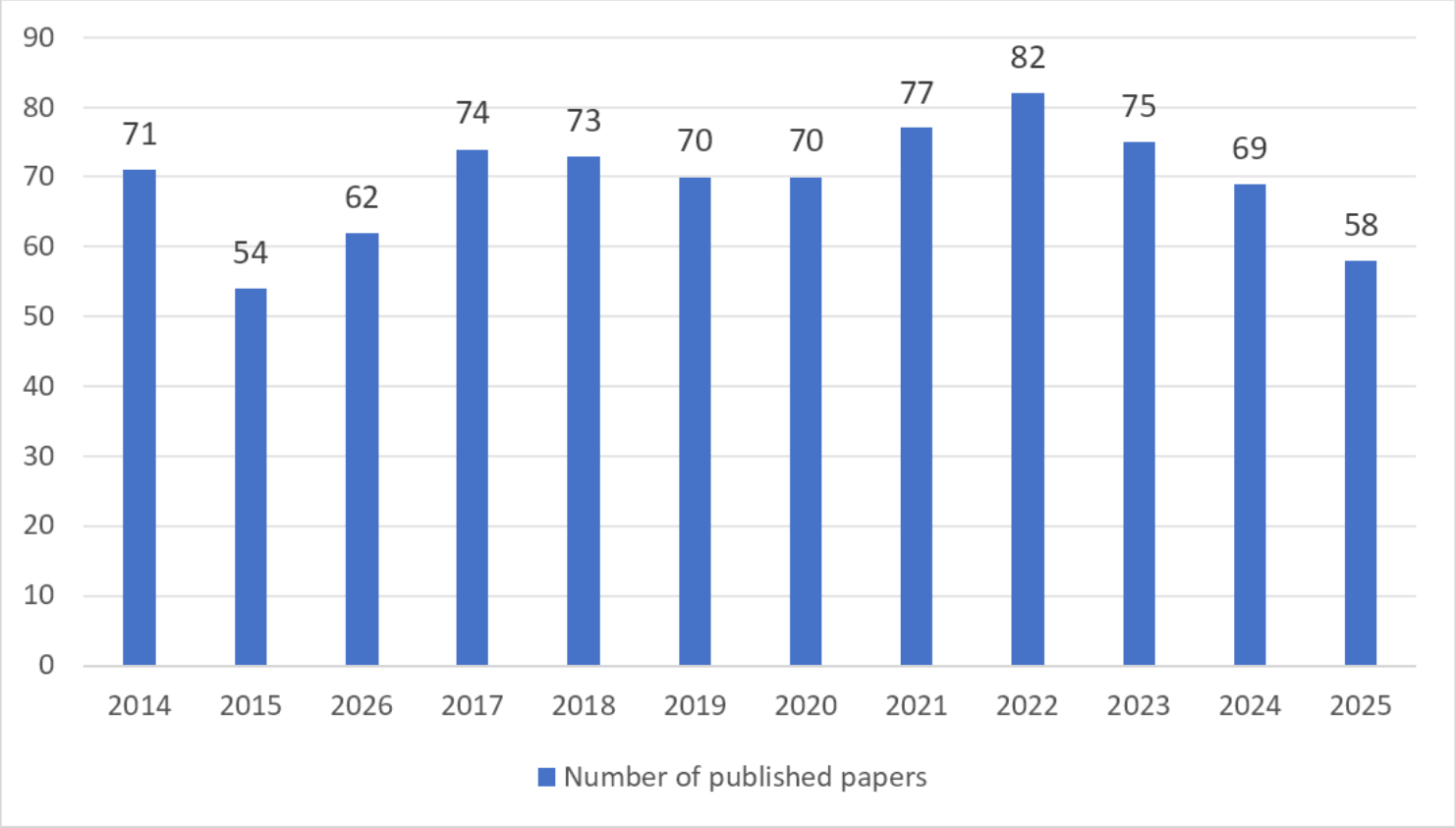


Figure 2

Temporal Trends in Spider Venom-Related Publication Output (2014-2025)

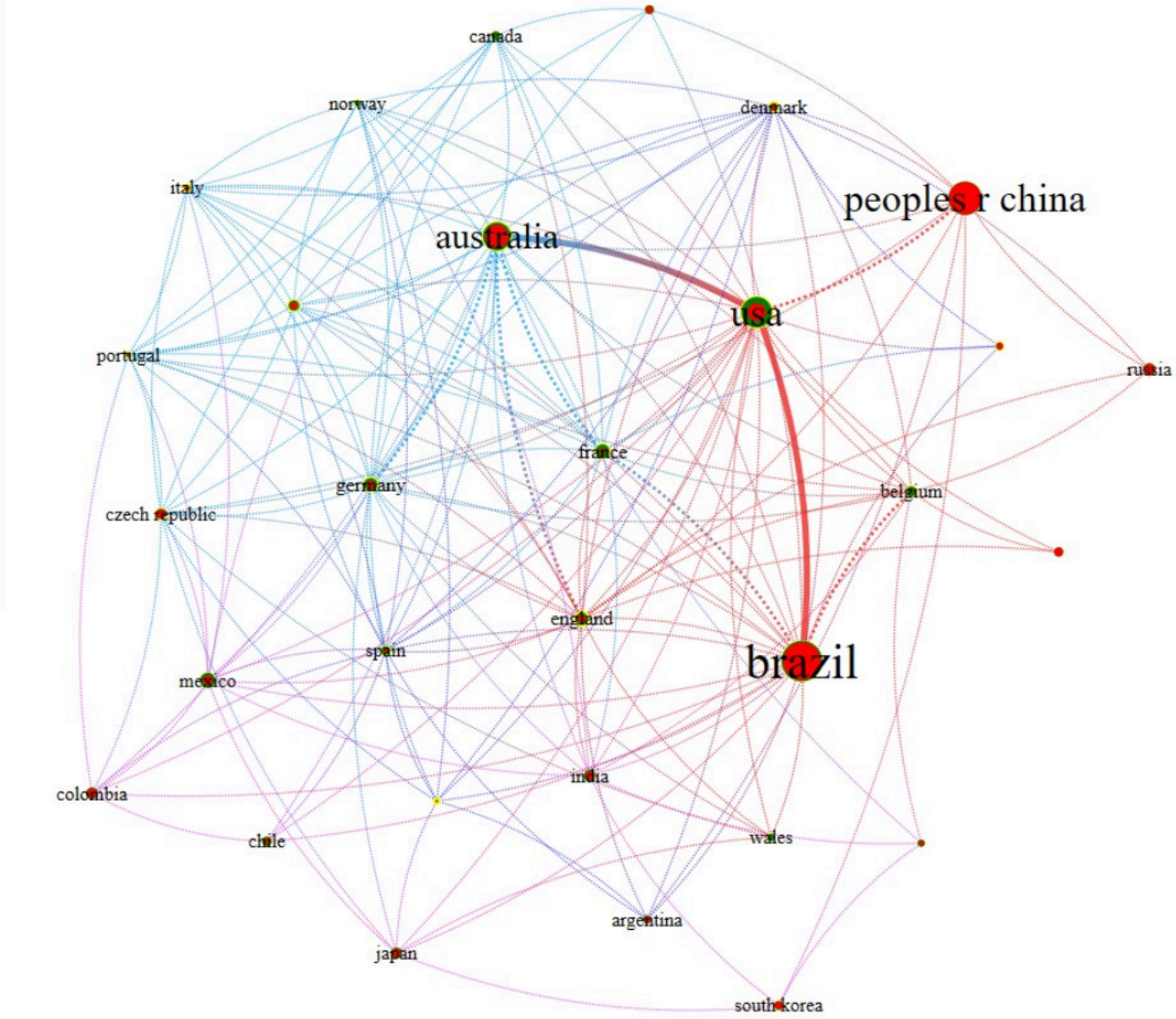


Figure 3

International Collaboration Network



Figure 4

Country Publication count

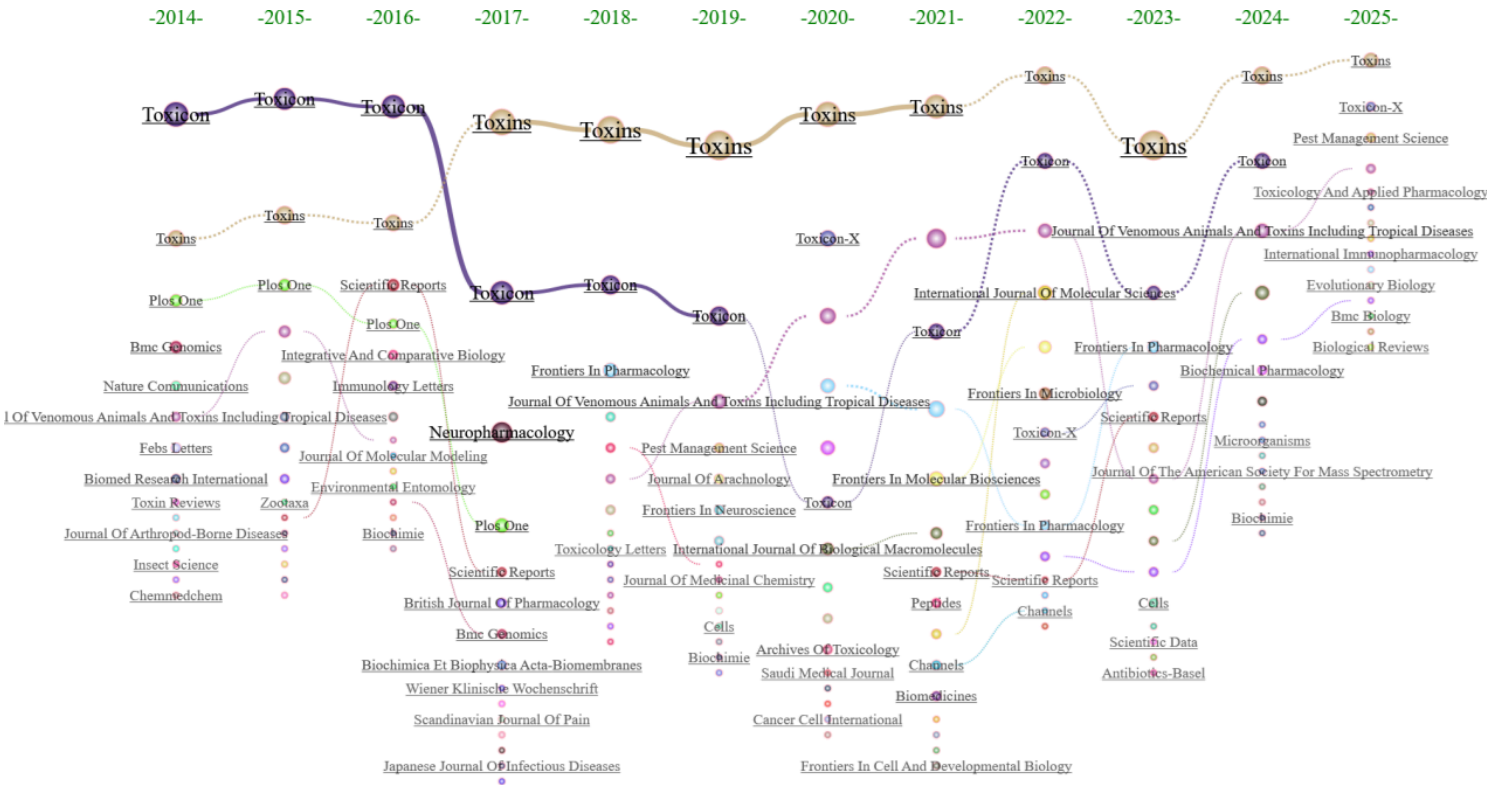


Figure 5

Evolution Publication graph

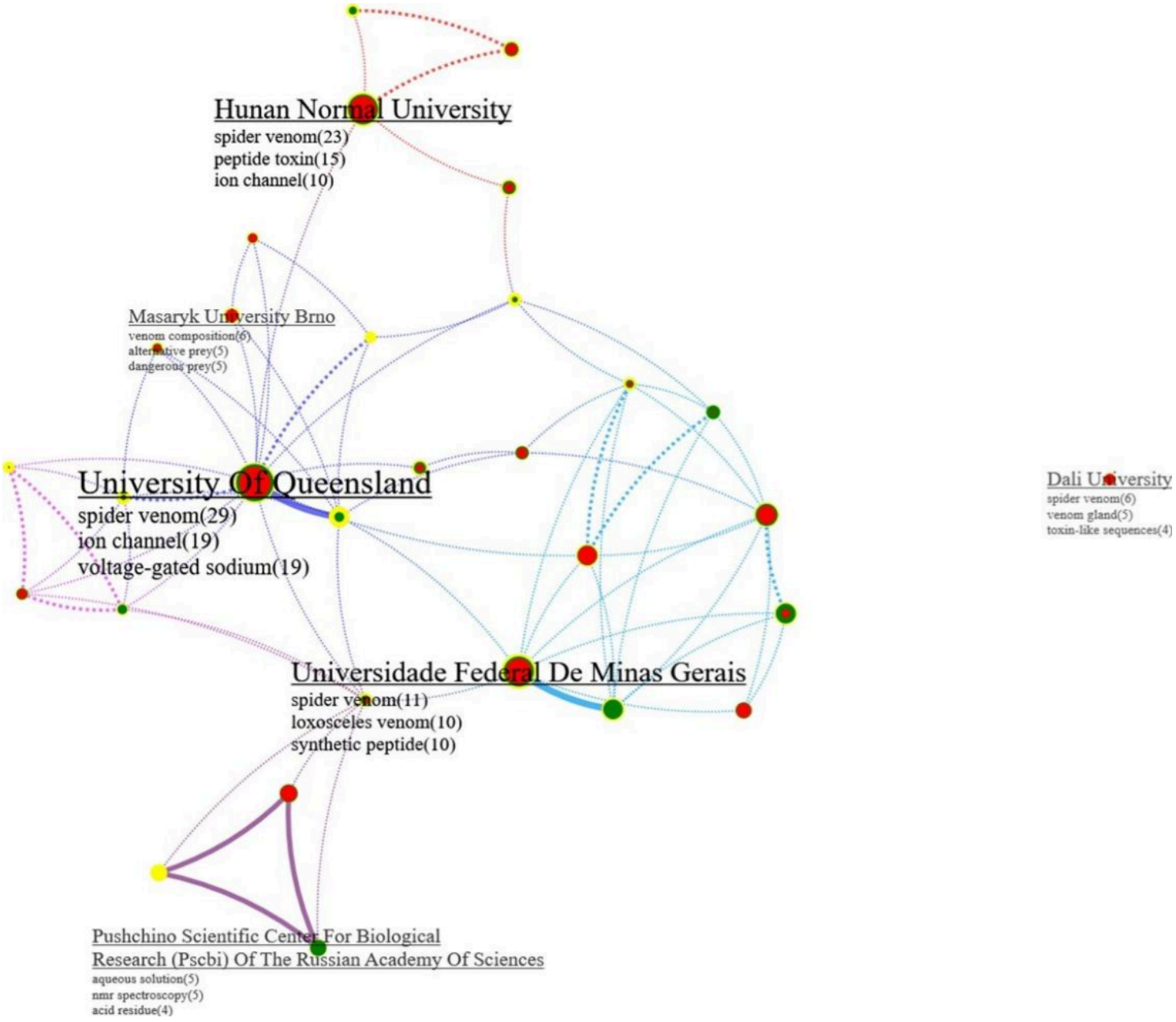


Figure 6

Co affiliation graph

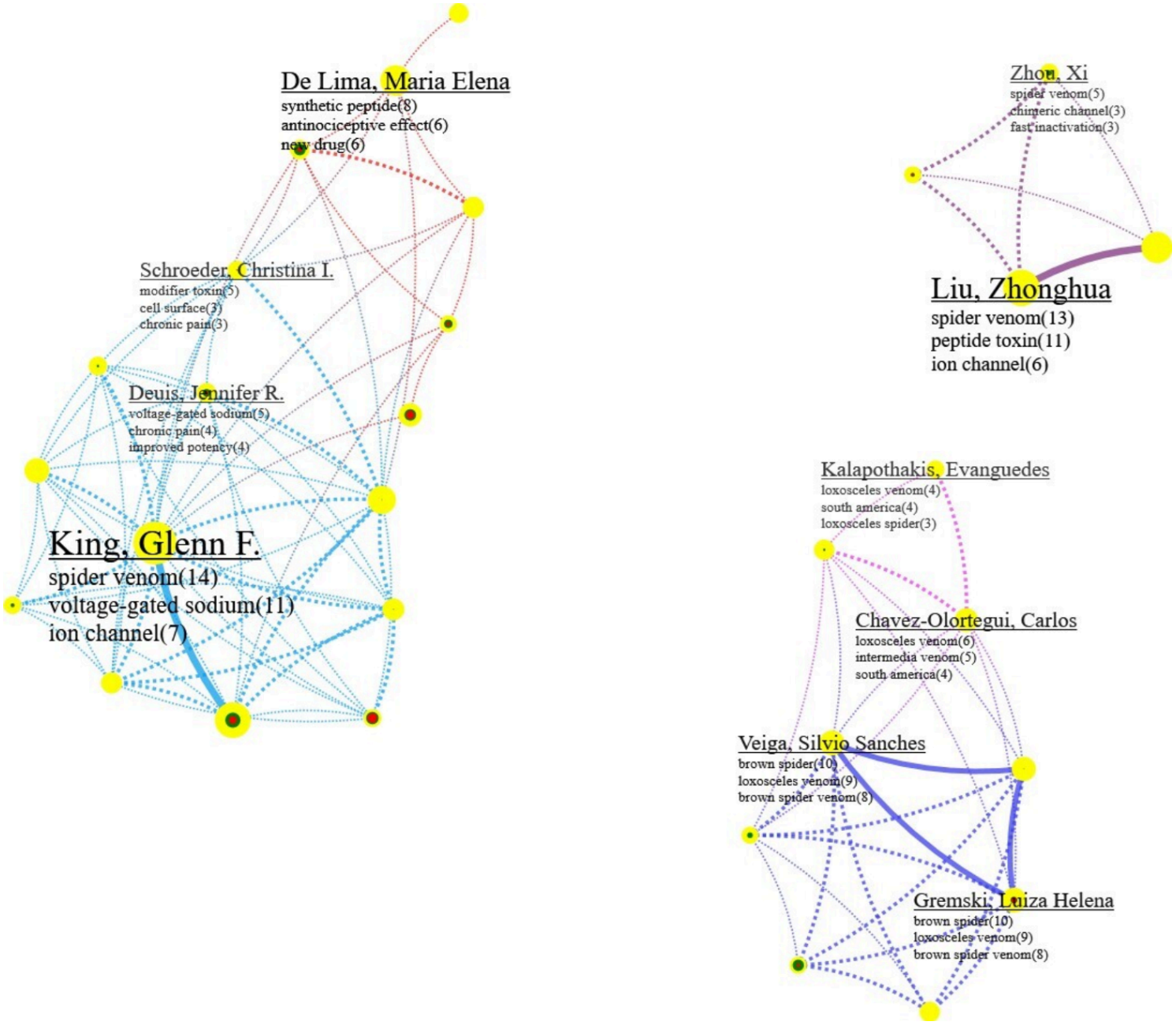


Figure 7

Co author graph

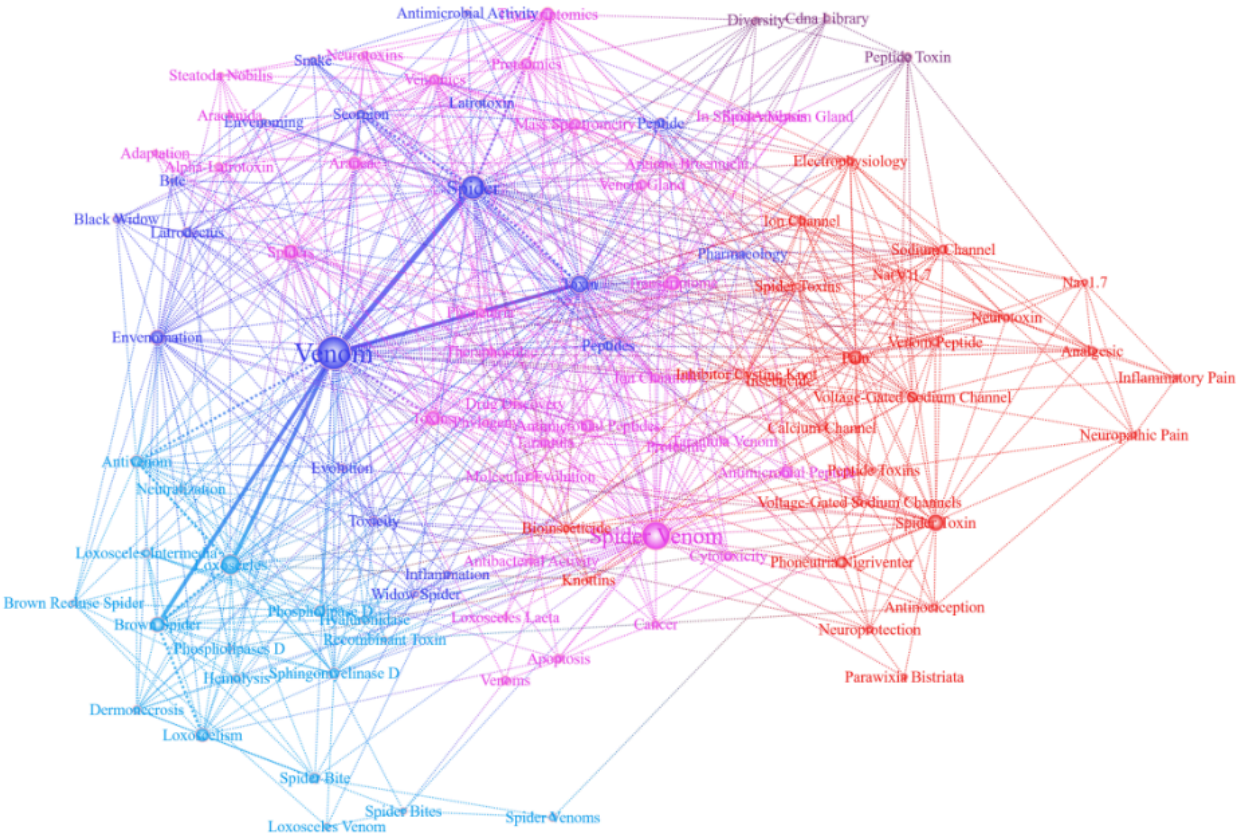


Figure 8

Keyword Co-occurrence Network Visualization

Supplementary Files

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