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Review Article

100 years of thiosemicarbazone: A bibliometric study using scopus database

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Abstract
Thiosemicarbazones (TSC) have received much attention in the scientific community due to their potential therapeutic applications, particularly in cancer and infectious disease treatment. This study aims to provide a comprehensive analysis of the global research trends, key contributors, and collaboration networks in TSC research. The bibliometric analysis utilizes a refined dataset of 6287 articles sourced from the Scopus database, covering the extensive period from 1922 to 2022. Based on the collected data, it can be determined that significant growth has occurred for the past century in TSC-related publications, especially in recent decades, with India, China, and the United States have emerged as major contributors to a substantial portion of the research output. In brief, this study provides valuable insights into global research dynamics, highlighting major contributors and emerging trends. Three most emerging trends discovered by this analysis are shift toward multifunctional therapeutic applications; development of metal complexes for enhanced bioactivity and globalization of research with growing contributions and collaborations. The implications of these findings underscore the importance of strategic partnerships and interdisciplinary approaches in propelling TSC research forward in the coming years. This study provides the first comprehensive, century-long analysis of global research trends on thiosemicarbazone (TSC), revealing its growing importance in therapeutic applications such as cancer and antimicrobial treatment. It identifies key contributors, emerging topics, and international collaborations, offering a valuable roadmap for future research. By visualizing data through bibliometric tools, the study supports evidence based decision making for researchers and institutions.

Keywords: thiosemicarbazone, bibliometric, research trends, scopus database

Introduction

Schiff bases are a class of organic compounds that are characterized by the presence of an imine group (C=N) in its composition. Since its first fabrication, the compounds have received much attention in the scientific community due to their biological characteristics that make them suitable for various applications. Specifically, when Schiff bases form complexes with metals, the resultant products will generally have higher effectiveness in terms of various biological actions, such as antibacterial, antifungal, antitumor, and anti-inflammatory properties 1. Historically, the initial synthesis route of Schiff bases, first described by Hugo Schiff in 1864, was performed by condensing primary amines with either aldehydes or ketones 1. These compounds act as adaptable ligands and can coordinate through the oxygen atom of the deprotonated phenolic group and the nitrogen atom of the azomethine group. In comparison, the stability of Schiff bases is higher when formed with aromatic aldehydes due to their extensive conjugation,

while those derived from aliphatic aldehydes are less stable and tend to polymerize rapidly.

Among the popular derivatives of Schiff bases, TSC stands out the most because of its extensive biological activities 2. Initially, TSC was recognized only for its metal-chelating capabilities. However, further analysis revealed its excellent performance in inhibiting the growth of tumors. The TSC molecular structure is composed of C=N and C=S bonds that are conducive to metal coordination, including a pliable thiourea framework, which allows for the materials incorporation of various substituents or functional group 3. For example, in regard to the heterocyclic ligands, the introduction of additional heteroatoms enhances the coordination mode of TSC and strengthens their metal-binding affinity 4. These compounds utilize an N–N–S donor system within their ligands to form stable complexes with transition metals. Previous studies suggest that such complexes exhibit superior antitumor activities compared to the individual ligands, both in vitro and in vivo 5. Furthermore, metal complexes are chemically and biologically diverse, a trait that cannot be inherited from their parent ligands. This diversity originates not only from variations in the metal and its oxidation state but also from the range of ligands that bind to the metal and the different coordination modes that have been adopted 2. Numerous researches have demonstrated that TSC ligands and their metal complexes have remarkable antitumor activities against various cancers, including lung, liver, colon, breast, neuroma, and others [7-10].

Despite the rapid surge in interest surrounding TSC research since its early development, a comprehensive global analysis of the research output for the past 100 years has yet to be conducted. While previous works on TSC have largely taken the form of systematic or traditional literature reviews, often focusing on biological applications or specific complexes, these studies lacked a holistic, data driven view of global research dynamics. This study uniquely addresses that gap by performing an extensive bibliometric analysis using a single, consistent source by using the Scopus database for over a century of literature. Recognizing the significance of such an analysis for future advancements, this study was performed with the aim of fostering collaboration and building networks among countries, academic institutions, and researchers. Unlike fragmented or narrowly scoped prior reviews, this analysis incorporates 6,287 curated journal articles and employs advanced mapping tools (e.g., VOSviewer) to reveal not only publication trends but also collaboration networks, keyword evolution, and thematic shifts across disciplines. By doing so, the study provides an unprecedented evidence based framework for understanding the evolution, hotspots, and future directions of TSC research worldwide. The Scopus database was selected as the exclusive source for data mining, as it provides the most extensive collection of abstracts and citation data across various peer-reviewed articles. This choice was made over other databases like Web of Science (WoS), PubMed, ScienceDirect, and the Directory of Open Access Journals (DOAJ) because the use of multiple databases could lead to confusion 10. The key objectives of this bibliometric analysis were to 1) evaluate the annual and cumulative trends in the publication of TSC-related journal articles; 2) identify the leading contributors in the field, including countries, academic institutions, journals, and authors; 3) explore the predominant terminology and topics based on author keywords and terms; 4) assess the influence of different countries on various TSC classifications; and 5) offer insights into potential research collaborations and future research directions. This study aims to assist researchers and stakeholders in identifying research gaps and staying informed about current trends in TSC research.

Methods

A bibliometric analysis offers a structured approach to comprehending and interpreting global publication trends. Unlike conventional review articles, this method draws on the collective focus derived from prior studies on a particular subject. Such an analysis can reveal numerous insights, including the future trajectory of the research area, notable accomplishments, ongoing challenges, existing limitations, and potential gaps that need to be addressed.

Data derivation and search procedures

Articles related to TSC were collected from the Scopus database in June 2022, with a focus on works published between 1922 and 2022. The extraction process started by entering specific terms like “thiosemicarbazone” in order to find the articles with only this term in their titles and abstracts. This step is crucial for a bibliometric study because the extracted data will serve as the foundation for further analysis. Then, the documents were filtered to include only journal articles, excluding irrelevant reviews, books, reports, and others. The search string used was: TITLE-ABS ((“thiosemicarbazone”) AND PUBYEAR > 1921 AND PUBYEAR < 2023 AND (LIMIT-TO (SRCTYPE, “j”)), which resulted in 6,317 documents. A second refinement step was carried out by adding terms like “review,” “revisit,” “critical,” “highlight,” “trends,” “scientometric,” and “bibliometric” to find any possible review papers and others that might be overlooked. This refinement led to the identification and removal of 94 publications. The removal process was done by excluding their EIDs, which, in turn, left a total of 6,287 documents.

In addition, it is important to note that the Scopus author I.D. (Scopus search code: AU-ID) is the most reliable identification method to accurately assess an author's publication output. This is because variations in an author's name across different journals can result in multiple profiles. If these profiles have not been merged, the Scopus database will treat them as separate entities.

To calculate the single-country publication (SCP), only the target country was included in the search results, while others were filtered out using the AFFILCOUNTRY field code. The ranking of the most notable journals and authors was determined by evaluating several indicators that are provided by Scopus, such as the h-index, total number of publications, CiteScore, total citations, and Field-Weighted Citation Impact (FWCI). Additionally, given the numerous applications and complexes of TSC today, two sub-themes were established to explore and illustrate global research interest in these areas. For each application and complex, modifications were made individually based on the initial search string of 6,287 articles, with additional terms included to narrow the scope. These terms encompassed antibacterial, antimicrobial, anticancer, antitumor, and antifungal for applications and copper, zinc, cobalt, nickel, and cadmium for complexes. The search results for each topic were then analyzed in terms of publication trends by year and the top five contributing countries. The data mining process and criteria for study exclusion are summarized in **Figure 1**, while the detailed search strings for both central and sub-themes are provided in Table S1 (Supplementary Material).

Bibliometric maps

Bibliometric maps based on the 6287 articles sourced from the Scopus database were generated using VOSviewer software (version 1.6.17). This software was chosen due to several advantages, such as extensive compatibility with various databases like PubMed, Web of Science, Lens, and Dimension, as well as free access. On top of that, the software allows manual customization of visual maps, which gives the users the freedom to adjust the items to represent countries and author keywords. Moreover, each item can be connected by lines with numerical values to reflect the strength of collaborative relationships between the two linked items. These relationships specifically indicate the total number of published articles shared between pairs of countries, referred to as items. In addition, a total link strength indicator is available to display the cumulative strength of co-authorship connections between one country and others. For the co-occurrence bibliometric maps, the numerical value of the links between two author keywords represents the count of publications, where both keywords were selected by the authors. The creation of both co-authorship and co-occurrence maps used a full counting system. Further information on the software's technical specifications is available in the instruction manual 12.

Analysis of co-authorship of countries

The analysis of co-authorship countries includes 110 countries with a total of 5987 affiliated authors. The countries on the map were displayed in a network visualization mode and clustered according to their continents: Asia, Europe, America, Africa, and Oceania.

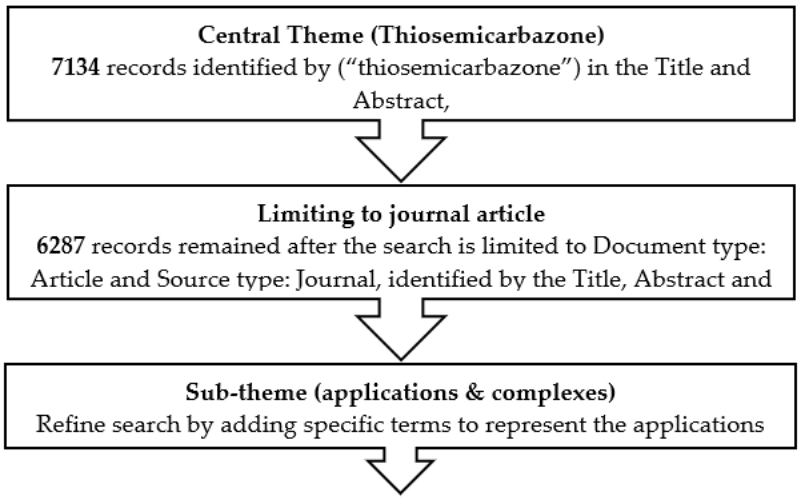


Figure 1. Research framework on the data collection process for primary and sub-themes

Analysis of co-occurrences of keywords and terms

The analysis of the co-occurrence of author keywords excluded those generated from Scopus indexing to ensure the precision of the selected articles. This is because, generally, the generated indexed keywords do not correctly represent the discussed topics of an article. Initially, 7,187 keywords were identified from the records. However, following a rigorous filtration process that aimed to reduce any redundancy, only 417 unique keywords remained. This process was performed by grouping together several synonymous keywords under a single term; for example, density functional theory (DFT), "DFT," "DFT calculation," and "DFT calculations" were all consolidated under "DFT calculation." These 417 keywords were further refined by applying a minimum occurrence threshold of five, using a full counting method. The final map of keyword co-occurrences was presented in an overlay visualization mode, which displayed the average publication year, occurrence frequency, and link strength of each keyword, represented by different colors.

TSC categories

A detailed comparison was performed to analyze the trends in yearly publications related to the central theme (keyword co-occurrences) and sub-themes (total publications). This comparison was designed to highlight the different focus of researchers on various applications and complexes of TSC. For example, one prominent application of TSC is its use as an antibacterial agent. To specifically target this application, modifications were made to the search query to collect articles that included both the keywords "thiosemicarbazone" and "antibacterial." On top of that, based on the cumulative publication output, the gathered articles revealed the top five leading countries in research on different TSC applications and complexes.

Results and Discussion

Publication trends and development of research interest

Throughout the 100 years (1922-2022) since its first publication, there have been 7134 articles published regarding TSC as the main research interest. Although the total number of publications is significant, the topic of TSC received limited attention during its first 30 years, as seen in the annual and cumulative distribution of articles in **Figure 2**. From 1922 to 1952, the annual publications on the topic never actually exceeded 8 articles, with a total of only 299 publications in this period. A major turning point in terms of the annual publication occurred in 1951 when a sudden spike in publications was observed. This event can be attributed to the recognition of TSC as an effective antitubercular agent, particularly with the development of thioacetazone during the period, which was extensively studied and used as part of tuberculosis treatment regimens 13. The next significant surge in publications occurred around 2003, which possibly stems from the advancements of the scientific community in the understanding of TSCs' anticancer properties. The discovery that TSCs, such as triapine, could inhibit ribonucleotide reductase, a key enzyme in deoxyribonucleic acid (DNA) synthesis, spurred considerable research interest in their potential as cancer therapeutics. This led to a marked increase in the number of studies published during this period 14.

Another notable increase in TSC-related publications was observed around 2013, and this surge can be linked to the growing interest in TSCs as multifunctional drugs that are capable of addressing a wide range of biological targets. In this period, the research saw significant advancements in the synthesis of novel TSC derivatives and their metal complexes. Among these advancements are the improved biological activities, including antimicrobial, antiviral, and anticancer properties. These developments further expanded the scope of TSC research, which, in turn, contributed to the rising number of publications. After 2005, the trend continued to grow, with 3,573 articles published from 2006 onwards, bringing the cumulative total to 6,287 publications by the most recent year in the dataset. This upward trajectory suggests that the research interest in TSC will likely persist as more ongoing research and the compound's expanding applications are made. Nonetheless, despite the considerable number of articles, challenges remain in terms of accessibility, as many of these publications may not be freely available, and this situation can potentially hinder broader dissemination and impact.

TSC research issue is becoming more extensive, with many researchers worldwide working tenaciously to improve its performance. The diversity of research and applications of TSC is evident based on the number of articles distributed across several subject areas, including Chemistry (4327; 68.82%), Biochemistry, Genetics and Molecular Biology (1520; 24.18%), Pharmacology, Toxicology and Pharmaceutics (1314; 20.90%), Materials Science (1207; 19.19%) and medicine (837; 13.22%). On top of that, the latest publications of TSC have shown that its application and interest in complexes has begun to be considered for other fields, such as Physics and Astronomy, Environmental Science and Agricultural and Biological Sciences. As for the publication language, the majority of the articles were published in English (5731; 91.15%), with some of them in German (105; 1.67%), Chinese (17; 0.27%), Italian (14; 0.22%), and Polish (11; 0.17%).

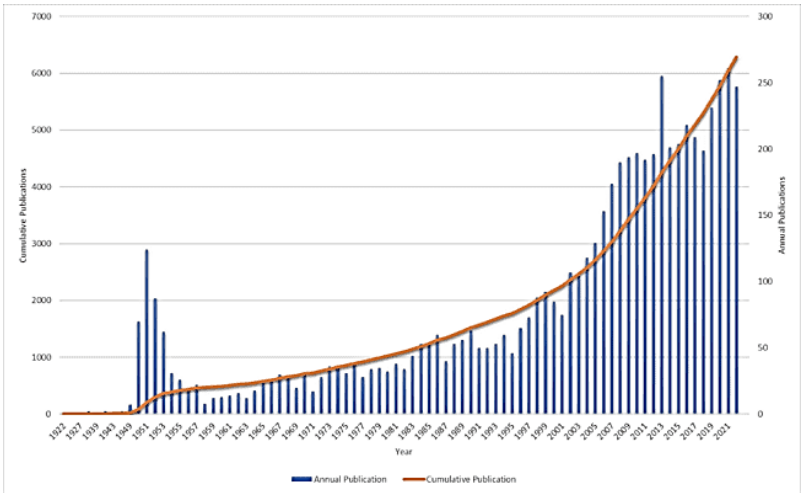


Figure 2. The distribution of annual and cumulative articles on TSC indexed in Scopus from 1922 to 2022

Productive journals

The list of the most productive journals based on the highest number of published articles in the TSC research area was tabulated in **Table 1**. Based on the tabulated information, these journals were generally owned by different publishers. However, compared to other publishers, Elsevier is considered to be most outstanding because the publisher's journals, such as "Polyhedron," "Journal of Molecular Structure," "Inorganica Chimica Acta," "European Journal of Medicinal Chemistry," and "Journal of Inorganic Biochemistry," represent a significant portion of the research output in the TSC field.

In terms of the publication output, as the most prolific journal with the highest number of publications, "Polyhedron" contributed a significant amount of 258 articles to the topic of interest, which covers about 4.11% of the total publications. This was followed by the "Journal of Molecular Structure" (161; 2.57%), "Inorganica Chimica Acta" (153; 2.44%), "Transition Metal Chemistry" (149; 2.37%), and "European Journal of Medicinal Chemistry" (139; 2.21%). Nevertheless, it must be noted that despite some journals being ranked lower in terms of the total number of articles published, some of them do demonstrate a significant impact based on their citation metrics. For instance, the most cited article from "Polyhedron" received 181 citations, with a notably high Field-Weighted Citation Impact (FWCI) of 9.86, suggesting that its influence in the research community is substantially above average. Other than that, the "European Journal of Medicinal Chemistry," although fifth in terms of its rank, managed to achieve a high FWCI of 6.56, with its most cited article receiving approximately 287 citations. This journal, along with others like the "Journal of Inorganic Biochemistry," which has a CiteScore of 7.0 and a most cited article with 232 citations, emphasizes the quality and impact of TSC research on the global scientific community. Similarly, "Inorganica Chimica Acta," third on the list, has a slightly lower FWCI of 1.75, yet its most cited article was referenced 189 times, which is an indicator of its relevance in the field. Springer Nature's "Transition Metal Chemistry" also stands out among the others, with 149 articles published, representing 2.37% of the total TSC publications. The journal's most cited article has 187 citations and an FWCI of 2.16, both of which reflect a strong impact relative to the number of articles published.

Additionally, the American Chemical Society's "Journal of Medicinal Chemistry" is another noteworthy journal on the list, with a moderate contribution of 104 articles (1.65%). Although it has a relatively lower number of publications compared to others, the journal possesses a high CiteScore of 12.3 and the highest number of citations (438) for its most cited article. This example shows that sometimes, the citation metrics can outweigh the total number of publications, especially when measuring a journal's impact. Other journals, such as the "Asian Journal of Chemistry" and "Synthesis and Reactivity in Inorganic and Metal Organic Chemistry," round out the list, though they show lower publication and citation metrics. The "Asian Journal of Chemistry," with 102 articles (1.63%), has the lowest CiteScore of 0.9 and an FWCI of 0.19. Similarly, "Synthesis and Reactivity in Inorganic and Metal Organic Chemistry," despite being in the tenth position with 93 articles (1.48%), has a modest FWCI of 1.09 and 48 citations for its most cited article.

In summary, even though most of the journals are ranked primarily based on the total number of

publications, other citation metrics, such as the CiteScore and FWCI, are believed to provide valuable insights into the quality and impact of the research published. Overall, "Polyhedron" leads the list not only in the number of articles but also in its remarkable citation impact. This is followed closely by other journals like the "European Journal of Medicinal Chemistry" and the "Journal of Medicinal Chemistry," which, despite fewer publications, demonstrate high impact through their citation performance. Therefore, researchers looking to contribute to the TSC field should consider both the quantity of articles published and the citation metrics when selecting a journal for publication.

Leading countries and prominent academic institutions for international network

Figure 3 shows the list of leading countries and their most prominent academic institutions in the field of interest. Based on the total number of publications, India led with 1,546 publications (26.7% of global output), with Guru Nanak Dev University as the most outstanding academic institution in the country with 75 published articles. The United States follows a bit far behind India with 909 publications (15.7%), with Illinois State University as its highest contributor with 127 published articles. Next, China ranks third with 501 publications (8.7%), dominated by the Ministry of Education of the People's Republic of China (45 articles). Spain (425 publications, 7.3%) and Universidad de Santiago de Compostela (172 articles) also make a significant impact on the tabulated list.

Meanwhile, Egypt (350 publications, 6.0%) is led by Mansoura University (71 articles), while Brazil (320 publications, 5.5%) has the Universidad Federal de Minas Gerais (108 articles) as its top institution. Turkey, with 248 publications (4.3%), is represented by Istanbul Üniversitesi (90 articles). Finally, the list was completed with Germany (204 publications, 3.5%), which stands out through Freie Universität Berlin (32 articles), and Australia (199 publications, 3.4%) and Italy (188 publications, 3.2%), which are led by The University of Sydney (92 articles) and Università di Parma (77 articles), respectively.

In regards to single-country publications, a parameter that determines the tendency of a country to have an international research collaboration, China and Turkey are on top of the list, with high SCP values of 88.6% and 85.1%, respectively, indicating minimal international collaboration. Other countries with more than 2/3 SCP include India (74.6%), Brazil (60.0%), and Egypt (56.0%). In contrast, Germany has the lowest SCP at 35.8%, highlighting significant international collaboration. In addition, Spain (54.6%), Australia (50.3%), and Italy (58.5%) showed moderate levels of international cooperation.

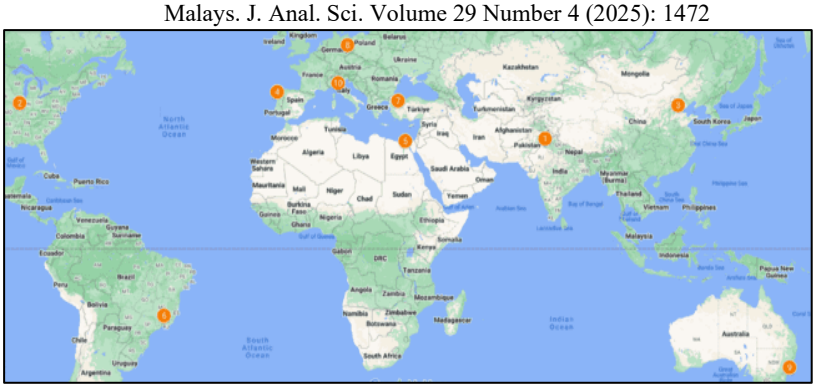
Figure 4 displays the co-authorship country map in network visualization mode. Each country was clustered according to its region/continent and linked based on international networks. There are several methods to understand the map: (1) a closer distance between the countries represents a stronger relatedness, (2) a thicker line means more publications were published through a collaboration between the two countries, and (3) different color indicates different clusters. The greatest number of countries per continent was Europe (38), followed by Asia (35), Africa (21), North/South America (13), and Oceania (3).

Additionally, according to the map, the United States has the highest number of affiliated countries, linked to 55 countries with 565 total link strength. Interestingly, in the second place, India, despite having the highest number of publications, was linked to 46 countries, with a total link strength of 524. The order was followed by Germany (43; 201), Spain (38; 289), France (38; 169) and Italy (34; 116). Furthermore, up to 52 countries (41.6%) on the list published less than 10 articles with a collaborative partnership from other countries.

Different factors, including the number and diversity of visiting scholars, wider research networks, funding in the form of grants from foreign resources, a large number of international postgraduate students, and others, influence the strength of global collaboration. As such, a country needs to have a flexible and tolerant policy towards outside researchers to improve the possibility of developing a robust international cooperation that can produce excellent research outputs for the benefit of humanity.

Table 1. The top 10 most productive journals on TSC research with their most cited article from 1922 to 2022. TP: total publication; FWCI: Field-Weighted citation impact

Rank	Journal	T.P. (%)	CiteScore (2022)	The Most Cited Article (Reference)	Times Cited	FWCI	Publisher
1	Polyhedron	258 (4.11)	5.4	Structural studies of three isomeric forms of heterocyclic N(4)-substituted thiosemicarbazones and two nickel(II) complexes 15	181	9.86	Elsevier
2	Journal of Molecular Structure	161 (2.57)	6.0	Bivalent transition metal complexes of coumarin-3-yl thiosemicarbazone derivatives: Spectroscopic, antibacterial activity and thermogravimetric studies 16	88	2.4	Elsevier
3	Inorganica Chimica Acta	153 (2.44)	5.6	Synthesis, structural characterization and biological activity of helicin thiosemicarbazone monohydrate and a copper(II) complex of salicylaldehyde thiosemicarbazone 17	189	1.75	Elsevier
4	Transition Metal Chemistry	149 (2.37	4.0	Antitumor activity of transition metal complexes with the thiosemicarbazone derived from 3-acetylumbelliferone 18	187	2.16	Springer Nature
5	European Journal of Medicinal Chemistry	139 (2.21)	12.1	Thiosemicarbazones, semicarbazones, dithiocarbazates and hydrazide/hydrazones: Anti-Mycobacterium tuberculosis activity and cytotoxicity 19	287	6.56	Elsevier
6	Journal of Inorganic Biochemistry	126 (2.00))	7.0	Synthesis, structural characterization and antimicrobial activities of 12 zinc(II) complexes with four thiosemicarbazone and two semicarbazone ligands 20	232	2.77	Elsevier
7	Spectrochimica Acta Part A Molecular and Biomolecular Spectroscopy	106 (1.69)	7.9	Spectral and magnetic studies on manganese(II), cobalt(II) and nickel(II) complexes with Schiff bases 21	134	2.41	Elsevier
8	Journal of Medicinal Chemistry	104 (1.65)	12.3	2-Acetylpyridine Thiosemicarbazones. 1. A New Class of Potential Antimalarial Agents 22	438	-	American Chemical Society
9	Asian Journal of Chemistry	102 (1.63)	0.9	Synthesis of some 2-amino-5-aryl-1,3,4-thiadiazoles 23	21	0.19	Asian Publication Corporation
10	Synthesis and Reactivity in Inorganic and Metal Organic Chemistry	93 (1.48)	-	Iron(III), cobalt(II), nickel(II), copper(II) and zinc(II) complexes of 4-formylantipyrine thiosemicarbazone 24	48	1.09	Taylor & Francis



Rank	Country	TPc	S.C.P. (%)	The Most Productive Academic Institution	TPi
1	India	1546	74.6	Guru Nanak Dev University	75
2	United States	909	55.9	Illinois State University	127
3	China	501	88.6	Ministry of Education of the People's Republic of China	45
4	Spain	425	54.6	Universidad de Santiago de Compostela	172
5	Egypt	350	56.0	Mansoura University	71
6	Brazil	320	60.0	Universidad Federal de Minas Gerais	108
7	Turkey	248	85.1	Istanbul Üniversitesi	90
8	Germany	204	35.8	Freie Universität Berlin	32
9	Australia	199	50.3	The University of Sydney	92
10	Italy	188	58.5	Università di Parma	77

Figure 3. The top 10 leading countries and academic institutions in the TSC research field

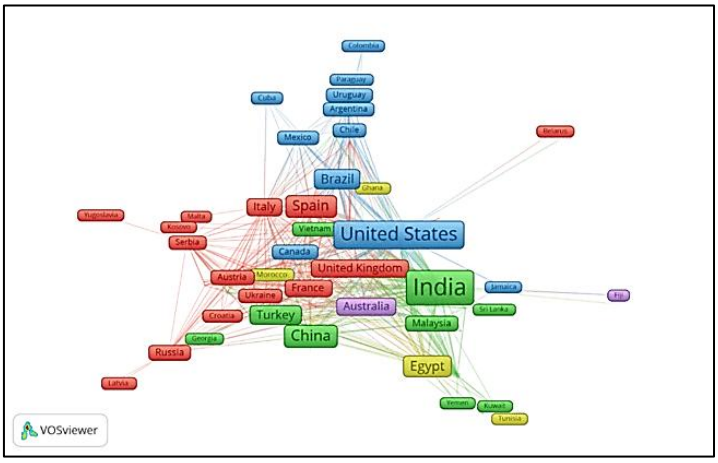


Figure 4. A bibliometric map fabricated according to the co-authorship in network visualization mode. The following uniform resource locator (URL) accessible online VOSviewer: https://bit.ly/3WQy3wY

Prolific authors

Table 2 presents the list of the most prolific authors in the TSC research field. According to the data, the selected authors were affiliated with universities in six different countries: the United States (3 authors), India (2 authors), Brazil (1 author), Japan (1 author), Turkey (1 author), Italy (1 author), and Spain (1 author). The data revealed that several researchers have had long-standing careers in this field, and their contributions, based on publications, can be traced back to the 1950s. The most experienced among them was A.C. Sartorelli, who began publishing in 1957, followed by D.X. West in 1967 and S. Chandra in 1977. The first publication year for these prolific authors ranges from 1957 to 1992. In terms of authorship roles, it is noteworthy that all authors have contributed significantly, either as first authors or co-authors, with a few holding supervisory roles that are typically indicated by their position as the last author in an article. The authorship arrangement, as presented, follows the Scopus database system without any subjective alterations to ensure an unbiased representation of each author's contributions. Nonetheless, readers are encouraged to assess the authors' impact using the provided metrics, such as total publications (T.P.), h-index, and total citations (T.C.).

When considering the number of publications per author, D.X. West, from the United States, led the list with 138 articles over nearly four decades. One notable aspect is that the last institution affiliated with D.X. West was in 2006 at the University of Washington. This might suggest that the author has already retired. Following him was D.R. Richardson, who is currently affiliated with Nagoya University, Japan, with 92 publications, and H. Beraldo, with 87 publications. However, while the total number of publications is an essential indicator of a researcher's productivity, the h-index, which balances productivity with citation impact, is a more comprehensive measure of influence in the academic community.

In this regard, D.R. Richardson stands out with an impressive h-index of 94, coupled with 5830 citations, making him the most influential author in this list. D.X. West also demonstrates substantial impact with an h-index of 50 and 6287 citations, while R.J. Butcher, with a slightly lower number of publications, holds an h-index of 62. Additionally, younger researchers like B. Ülküseven from Turkey, despite having a shorter publication history starting in 1992, have made notable contributions with 73 publications, an h-index of 24, and 1131 citations, indicating a promising career trajectory in TSC research.

Co-occurrences of author keywords

Out of 7187 author keywords that were exported from the Scopus database, only 417 keywords met the threshold for the mapping process in VOSviewer software when the minimum of occurrences was set to 5. Several filtrations and re-labeling procedures were performed during the selection to ensure that these keywords are not synonymous and congeneric.

Terminology and concept

Our results on the co-occurrence of author keywords analysis in Figure 5 showed that 'thiosemicarbazone' was the most frequently used, with 1557 occurrences and linked to 371 other keywords. The result is within expectation since TSC is a popular sub-discipline under both chemistry and biology. The sequences were followed by 'crystal structures' (254 occurrences; 168 links), 'cytotoxicity' (190 occurrences; 146 links), 'synthesis' (144 occurrences; 123 links), and 'antimicrobial activity' (134 occurrences; 96 links). The high interest in 'thiosemicarbazone' as a key research topic is likely due to its potential therapeutic properties, affordability, versatility in chemical synthesis, and ease of handling and storage. Currently, key companies and institutions involved in thiosemicarbazone research and production include Sigma-Aldrich (part of Merck Group), which supplies various TSC derivatives for research purposes, AstraZeneca and Novartis, both exploring TSC compounds for cancer therapy, Alfa Aesar (a Thermo Fisher Scientific company), which provides thiosemicarbazones for pharmaceutical research, and Vion Pharmaceuticals, known for conducting clinical trials on Triapine, a TSC derivative with anticancer

Table 2. List of the most prolific authors in the TSC research area

	Author	Scopus Author ID	Year of 1st Publication*	TP	h-Index	T.C.	Latest Affiliation	Country
1	West, D.X.	7401998112	1967[a]	138	50	6287	University of Washington (2006)	United States
2	Richardson, D.R.	7403445073	1988[a]	92	94	5830	Nagoya University	Japan
3	Beraldo, H.	7003871376	1983[a]	87	43	2945	Federal University of Minas Gerais	Brazil
4	Chandra, S.	56216186000	1977[a]	73	43	1415	University of Delhi	India
5	Lobana, T.S.	35510467100	1981[a]	73	34	1836	Guru Nanak Dev University	India
6	Ülküseven, B.	6601984987	1992[b]	73	24	1131	Istanbul University-Cerrahpasa	Turkey
7	Butcher, R.J.	7201947292	1975[a]	64	62	1934	Howard University	United States
8	Pelosi, G.	7102464332	1989[b]	60	43	2798	University of Parma	Italy
9	Castiñeiras, A.	7006710796	1978[b]	52	51	1330	University of Santiago de Compostela	Spain
10	Sartorelli, A.C.	36039619900	1957b	51	68	2266	Yale University (2018)	United States

* Role in co−authorship, superscripts

potential. The popularity of TSC applications and complexes was followed by 'molecular docking' and 'antibacterial activity' with 108 and 102 occurrences and 94 and 83 links, respectively. Besides that, copper has high occurrences in numerous research fields because of its unique property as a TSC complex that enhances its biological activity, particularly in anticancer and antimicrobial applications. This property allows copper-TSC complexes to act as potent inhibitors of key enzymes involved in cancer cell proliferation.

Moreover, we also found out that the most important characteristics of TSC highlighted by the researchers were 'antioxidant' (54 occurrences), 'antifungal' (43), 'anticancer' (39), 'anti-inflammatory' (20), 'antitumor' (19), 'antiproliferative' (17) and 'antiviral' (10). Several keywords also corresponded to the instruments and techniques used for the characterization purposes of TSC. Some of the lists were 'DFT' (95 occurrences; 107 links), 'X-ray Diffraction' (51 occurrences; 64 links), 'EPR Spectroscopy' (28 occurrences; 37 links), 'QSAR' (23 occurrences; 25 links), 'EIS' (18 occurrences; 12 links), 'NMR spectroscopy' (11 occurrences; 13 links), 'in vitro' (7 occurrences; 13 links). As for the complexes, several keywords were discovered to represent them. For example, the keyword 'Ni(II) complexes' occurred 46 times, 'Cu(II) complexes' (15), 'Cobalt(III) complexes (13), 'Zn(II) complexes' (11), 'Tin(IV) complexes' (8), and 'Pd(II) complexes' (7).

Within the extensive collection of author keywords, only a select few were marked in yellow, signaling that these terms reflect the most current focus areas in TSC research. Notable among them are 'molecular docking,' 'DNA/protein binding,' 'Hirshfeld surface analysis,' 'A549 cells,' 'iridium,' and 'rhodium.' These significant keywords provide valuable insight and direction for upcoming research endeavors, helping to align them with the latest trends in the field.

Distribution of TSC based on different applications and complexes

Limitation of study

The study primarily relies on bibliometric analysis using data extracted from the Scopus database. While Scopus is comprehensive, it does not include all relevant scientific literature. Therefore, some articles might be potentially excluded due to the studies being published in non-indexed journals. Additionally, the focus on publications with the keyword "thiosemicarbazone" may have excluded relevant research that did not explicitly mention this term. Moreover, the reliance on automated keyword co-occurrence and author affiliation data also introduces the possibility of inaccuracies due to variations in author names and affiliations. Other than that, the study's exclusion of non-English language publications may result in a skewed representation of global research trends and underrepresented contributions from non-English speaking countries.

Conclusion

This study significantly advances the body of knowledge on thiosemicarbazones (TSCs) by providing a comprehensive bibliometric analysis of 6,287 publications indexed in the Scopus database from 1922 to 2022. In addition, the growth in publications, particularly in recent decades, indicates a rising interest in TSCs due to their potential applications in fields such as pharmacology, chemistry, and biochemistry. The data suggests that TSC research is likely to continue expanding as researchers explore new therapeutic applications and chemical properties. Besides, we identified key contributors to this field, including countries like India, China, and the United States, along with leading academic institutions to provide a foundation for future international collaborations. This study also highlighted several significant advancements in TSC research, especially in the development of TSCs as antitumor and antimicrobial agents, which could serve as a focal point for future studies.

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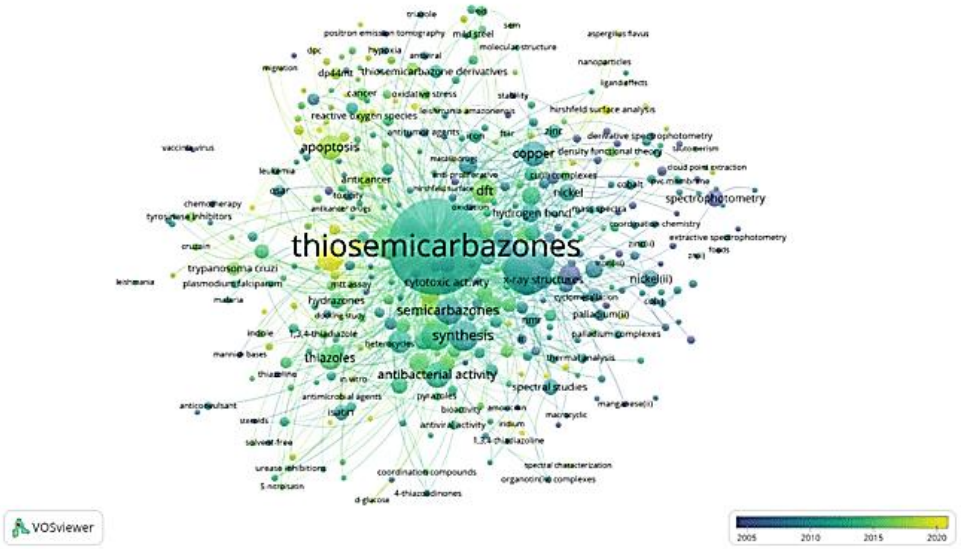

Figure 5. A bibliometric map fabricated according to the author's keywords co-occurrence in overlay visualization mode. The following URL can be used to open Figure 5 in online VOSviewer: https://bit.ly/4dOM05

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