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Review Article

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A Bibliometric Overview of Exerkines: Uncovering the Hidden Benefits of Exercise Training and Physical Activity

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Abstract

Background: Exerkines, bioactive molecules released during physical activity, are key mediators of exercise-related health benefits, including disease prevention, health promotion, and enhanced resilience. Despite their significance, no bibliometric analysis of exerkine research has been conducted. **Method:** This study aims to provide a comprehensive bibliometric overview of exerkine studies from 2016 to 2024, using the Web of Science database. We analyzed 131 publications through the Bibliometrix R package and VOSviewer to explore publication trends, key contributors, and research hotspots. **Results:** Results show a 55.39% annual growth rate, with 87 journals publishing in this field, led by Frontiers in Physiology. China and the USA contributed the most publications. High-frequency keywords included skeletal muscle, physical activity, and insulin resistance, reflecting core research areas. Ewa Ziemann was the most prolific author. **Conclusion:** This analysis highlights global research trends, influential journals, and emerging themes, offering a foundation for future investigations. By mapping the current state and potential directions of exerkine research, this study supports researchers in advancing knowledge and optimizing exercise-based interventions.

Keywords: bibliometric analysis, exercise training, physical activity, exerkines

Introduction

There is ample evidence that regular physical activity offers numerous health benefits, including increased lifespan, improved overall health, and the prevention of various diseases (Piercy et al., 2018). Individuals who engage in regular physical activity tend to have a lower incidence of chronic and degenerative diseases (Marques-Aleixo et al., 2020). They are also at a reduced risk of developing serious metabolic disorders, such as type 2 diabetes, metabolic syndrome, and fatty liver disease. Additionally, maintaining an active lifestyle can help delay age-related health issues (Piercy et al., 2018; Seo et al., 2019). Although the mechanism by which exercise training affects health is not fully understood, further investigation is needed. In recent decades, researchers have made significant progress in elucidating the diverse cellular and molecular pathways activated throughout the body during exercise, aiming to understand the beneficial biological effects of physical activity on health. At the biochemical level, exercise stimulates the release of signaling molecules known as exerkines from various organs, which perform their functions through autocrine, paracrine, and endocrine processes (Lisa S Chow et al., 2022; Türkel et al., 2022; Westphal, 2023).

Exerkines are broadly defined as bioactive molecules and humoral factors released from multiple organs and tissues in response to acute or chronic physical activity. These molecules act through autocrine, paracrine, and endocrine mechanisms and include myokines from skeletal muscle, hepatokines from the liver, adipokines from adipose tissue, cardiokines from the heart, batokines from brown adipose tissue, and neurokines from the nervous system (Lisa S. Chow et al., 2022; Novelli, Calcaterra, Casciani, Pecorelli, & Mehta, 2024). This diverse group encompasses cytokines, peptides, nucleic acids (such as miRNAs and mtDNA), lipids, and metabolites, frequently transported via extracellular vesicles (Vechetti Jr, Valentino, Mobley, & McCarthy, 2021).

The first identified exerkine was interleukin-6 (IL-6), which rapidly increases in circulation following exercise. Subsequent studies have identified additional key exerkines such as IL-15, irisin, myonectin, FGF-21, and apelin, each playing distinct roles in metabolic regulation, inflammation, and inter-organ crosstalk (Jin, Diaz-Canestro, Wang, Tse, & Xu, 2024; Piccirillo, 2019). For this bibliometric analysis, we adopted this inclusive definition to capture the full spectrum of exercise-induced signaling molecules beyond the traditional focus on myokines.

Bibliometric analysis is a relatively new branch of information science which helps in understanding the conceptual framework of knowledge fields. Through bibliometric studies, researchers can determine the major themes of research in a specific area. In addition, bibliometric analyses are commonly used to identify important articles and landmark publications which have had a profound effect on the scholar's community.

While previous bibliometric studies have primarily focused on individual exerkines such as irisin or the myokine family (Gao et al., 2025; Sun et al., 2024), no comprehensive bibliometric analysis has yet mapped the broader and rapidly evolving field of exerkines as a unified conceptual framework. This gap is particularly timely to address, given the substantial growth in exerkine research since 2021 and the increasing recognition of these molecules as key mediators linking exercise to disease prevention, metabolic health, and resilience across multiple organ systems. The present study fills this conceptual and mapping gap by providing a systematic bibliometric overview of exerkine literature from 2016 to 2024. It elucidates publication trends, international collaborations, influential contributors, and emerging research hotspots to guide future investigations in exercise physiology.

Methods

Searching strategy and data collection

Data were obtained from the Web of Science Core Collection (WoSCC) database on November 28, 2024. This most impactful scientific database includes journals that are regarded as high-quality and are frequently utilized for bibliometric analysis within the health and medical sectors (Merigó & Núñez, 2016; Zhu & Liu, 2020). The search strategy was constructed as follows: (((TS=(exercise)) OR TS=("exercise training")) OR TS=("physical activity")) AND TS=(exerkine*) Publications were restricted to the period from January 1, 2016, to November 28, 2024. Only original articles and review articles were included; other document types (e.g., conference papers, editorials, letters, and comments) were excluded. No language restrictions were applied. The wildcard () was applied to "exerkine" to include variations such as exerkine and exerkines. After retrieval, duplicate records were automatically removed by the Web of Science platform. Two independent reviewers manually screened all titles and abstracts for relevance, with disagreements resolved by consensus or a third reviewer. Full texts were obtained for all potentially eligible records. Figure 1 illustrates the detailed flowchart of the publication selection process following PRISMA guidelines adapted for bibliometric studies.

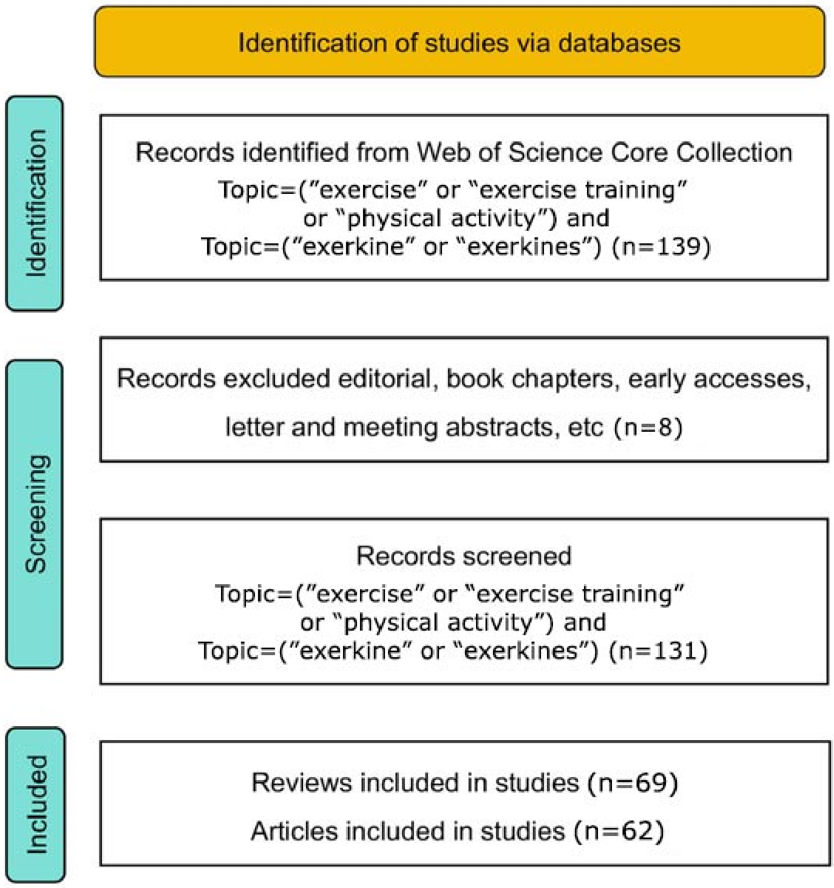

Figure 1. Flowchart of the publication selection.

Data analysis and visualization

The bibliometric analysis in this research utilized various software tools for distinct purposes. For the quantitative analysis, R-Studio, a free and open-source development environment for R, was employed on the Windows operating system. The Bibliometrix package was specifically used for data analysis and interpretation (Derviş, 2019). The VOSviewer software (version 1.6.20) developed by Leiden University in the Netherlands was utilized for mapping and visualizing co-occurrence networks (Van Eck & Waltman, 2010). In the network map generated by VOSviewer, the size of the nodes indicated the number of articles or the frequency of co-occurrence, while the different colors of the nodes represented various categories of research topics. The connections between nodes illustrated their co-occurrence relationships, with the thickness of the links reflecting the frequency of co-occurrence between the two nodes.

Results

Publication Output Analysis

Among the 131 documents analyzed, 62 (52.67%) were articles, while 69 (47.33%) were review articles. The annual distribution of publications, shown in Figure 2, demonstrates a steady upward trend, with a slight decline in 2024. Notably, there was a substantial increase in publications following 2021, reflecting ongoing developments in the field.

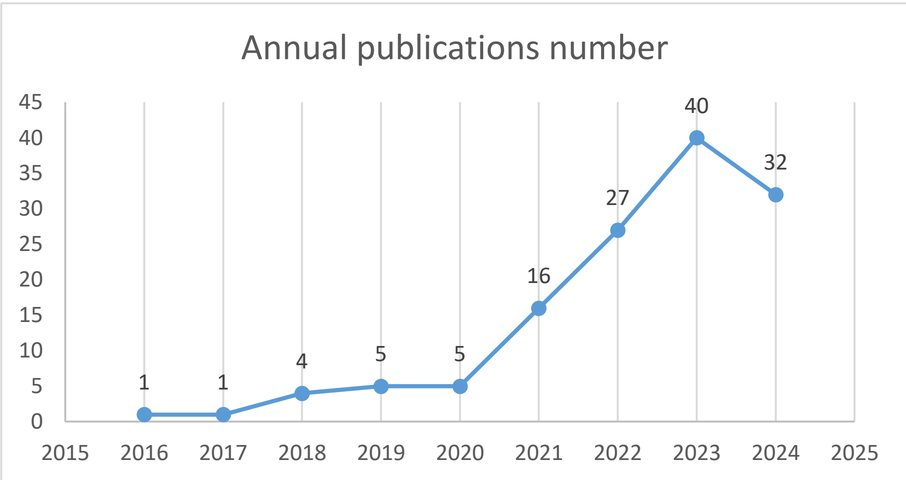

Figure 2. Annual number of publications from 2016 to 2024.

Analysis of countries/regions and institutions

37 countries and regions, along with 354 institutions, contributed to the publication of 131 papers. Table 1 lists the leading 10 countries and regions for publications. China had the highest publication count during

the study period, with 32 papers (24.42%), followed by the United States with 28 (21.37%) and Canada with 15 (11.45%). The top 10 countries and regions accounted for over 66.00% of all papers, indicating a disparity in research development across different areas (Figure3).

Table 2 shows the top 10 institutions in terms of publications in the field. Shanghai University of Sport (n=9, 6.87%), McMaster University, and the Poznan University of Physical Education (n=7, 5.34%) had the highest number of publications during the study period, followed by Gdansk University of Physical Education Sport, the University of California system, and the university of Copenhagen (n=6, 4.58%).

Table 1. Top 10 countries/regions by number of publications.

Rank	Countries/Regions	Publications	n (%)
1	China	32	24.42
2	Usa	28	21.37
3	Canada	15	11.45
4	Italy	11	8.39
5	Poland	11	8.39
6	Australia	10	7.63
7	Germany	7	5.34
8	Brazil	6	4.58
9	Denmark	6	4.58
10	France	6	4.58

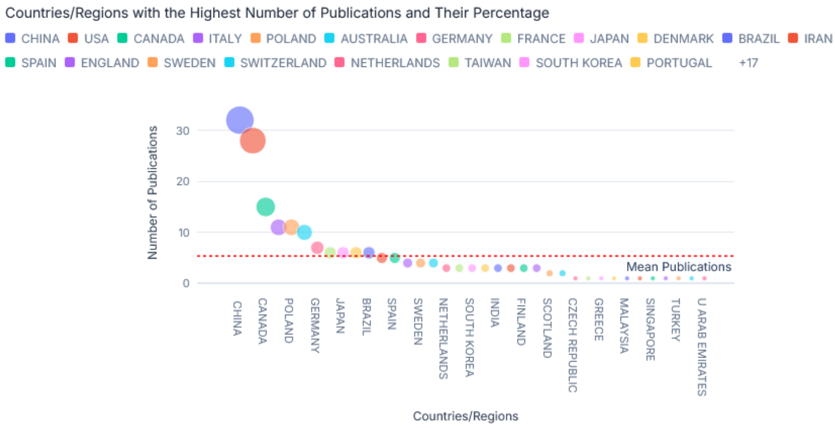

Figure 3. Countries/regions with the highest number of publications.

Table 2. Top 10 institutions by number of publications.

Rank	Institutions	Publications	n (%)
1	Shanghai University of Sport	9	6.87
2	Mcmaster University	7	5.34
3	Poznan University of Physical Education	7	5.34
4	Gdansk University of Physical Education Sport	6	4.58
5	University of California System	6	4.58
6	University of Copenhagen	6	4.58
7	Shaanxi Normal University	5	3.81
8	Ciber Centro De Investigacion Biomedica en Red	4	3.05
9	Fahrenheit Universities	4	3.05
10	Louisiana State University	4	3.05

Analysis of journals and categories

All the retrieved publications were published in 87 different journals. We visualized all the Relevant journals regarding the number of publications (Figure 4). Table 3 presents the top 10 journals in this field. The five journals with the highest number of publications are as follows: Frontiers in Physiology (n=12, 9.16%), International Journal of Molecular Sciences (n=6, 4.58%), Frontiers in Endocrinology (n=5, 3.81%), Cells (n=4, 3.05%), and Journal of Sport and Health Science (n=4, 3.05%). Among the top 10 journals, Frontiers in Physiology had the most citations, with 344 citations, while Nature Reviews Endocrinology had the highest number of citations, with 652 citations. The leading five categories in the Web of Science for this area include Physiology (n=25, 19.08%), Biochemistry and Molecular Biology (n=24, 18.32%), Endocrinology and Metabolism (n=20, 15.26%), Sport Sciences (n=18, 13.74%), and Cell Biology (n=17, 12.97%).

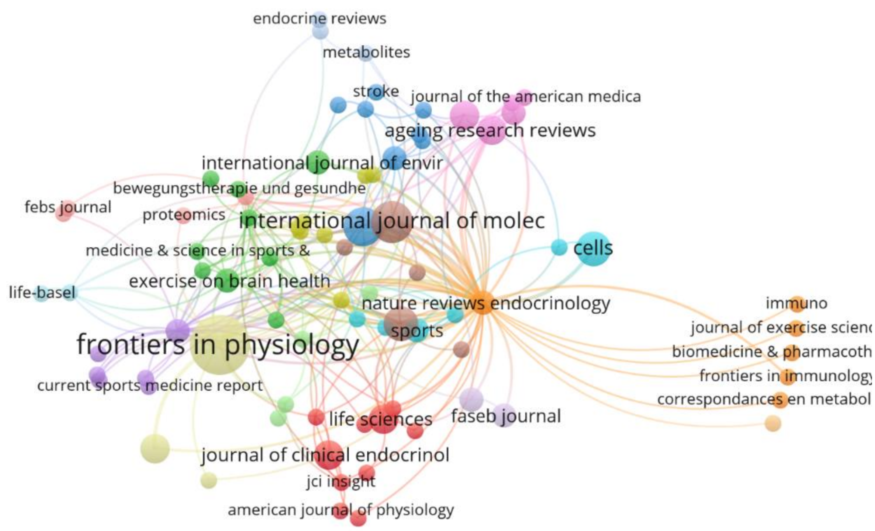

Figure 4. Visualization map of all the relevant journals.

Table 3. Top 10 journals by number of publications.

Rank	Journal	Publications	Citations	IF
1	Frontiers in Physiology	12	344	4.1
2	International Journal of Molecular Sciences	6	149	4.9
3	Frontiers in Endocrinology	5	21	6.0
4	Cells	4	35	5.1
5	Journal of Sport and Health Science	4	166	9.7
6	Ageing Research Reviews	3	21	12.5
7	Journal of Applied Physiology	3	16	3.3
8	Journal of Clinical Endocrinology Metabolism	3	2	5.0
9	Life Sciences	3	6	6.7
10	Progress in Biochemistry and Biophysics	3	0	0.2

Analysis of Authors and Coauthorship Networks

In the field of exercise and exerkines, a total of 733 authors have contributed to the literature. We created a visualization network with the top 66 authors based on the collaborative relationships. (Figure 5). The authors with the highest number of publications are Ewa Ziemann from Poznan University (n=6, 4.58%), Zhenjun Tian from Shaanxi Normal University (n=5, 3.81%), and Katarzyna Micielesca from Poznan University (n=4, 3.05%). Table 4 presents the top 10 authors in terms of the number of published papers.

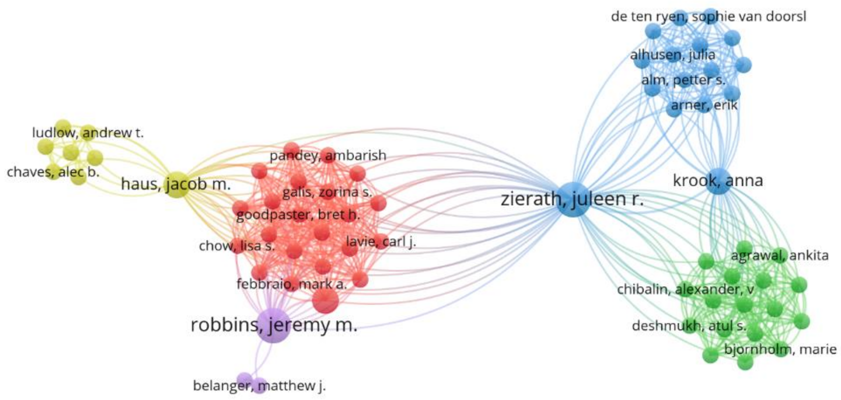

Figure 5. Visualization of research networks of authors.

The analysis of collaboration among all authors revealed that only 66 authors, accounting for 9.00%, formed a collaborative network, which was divided into five main clusters. The thickness of the lines in the network indicates the strength of the relationships between authors. The largest cluster, represented in red, included 22 authors (33.33%) and centered around Lisa Chow, Mark Febbraio, Amarish Pandey, Carl Lavie, Bret Goodpaster, and Zorina Galis. The second cluster, shown in green, was led by Agrawal, Chibalin, and Bjornholm, who had the largest nodes and were the most active co-authors in the field. The smallest cluster, depicted in purple, comprised only three authors (4.53%), but they collaborated with members of the largest cluster and with authors who had a high number of publications. Meanwhile, there was a noticeable lack of collaboration among the other top ten authors involved in research in this publication field.

Table 4. Top 10 most productive authors

Rank	Authors	Publications	n (%)
1	Ziemann E	6	4.58
2	Tian ZJ	5	3.81
3	Micielska K	4	3.05
4	Tarnopolsky MA	4	3.05
5	Zhang X	4	3.05
6	Feng LL	3	2.29
7	Jaworska J	3	2.29
8	Jia DD	3	2.29
9	Kozlowska M	3	2.29
10	Li BW	3	2.29

Analysis of keywords

Keywords are essential for analyzing the knowledge structure of an academic field from a bibliometric perspective, aiding in identifying potential research hotspots. Figure 6 displays a cloud map of the top 50 keywords identified in these articles, with bolder fonts indicating a higher frequency of occurrence. The most frequently used keywords include “skeletal muscle” (n = 32), “physical activity” (n = 31), “aerobic exercise” (n = 24), “exercise” (n = 19), “neurotrophic factor” (n = 19), “adipose tissue” (n = 14), “expression” (n = 14), “gene expression” (n = 14), “insulin resistance” (n = 14), “physical exercise” (n = 14), “human skeletal muscle” (n = 13), “insulin sensitivity” (n = 11), "oxidative stress" (n = 10), and "synaptic plasticity" (n = 10), all of which occurred more than 10 times. The evolution of these key terms over time is illustrated in Figure 7.

Figure 6. Cloud map of high–frequency keywords in the field of exercise and exerkines.

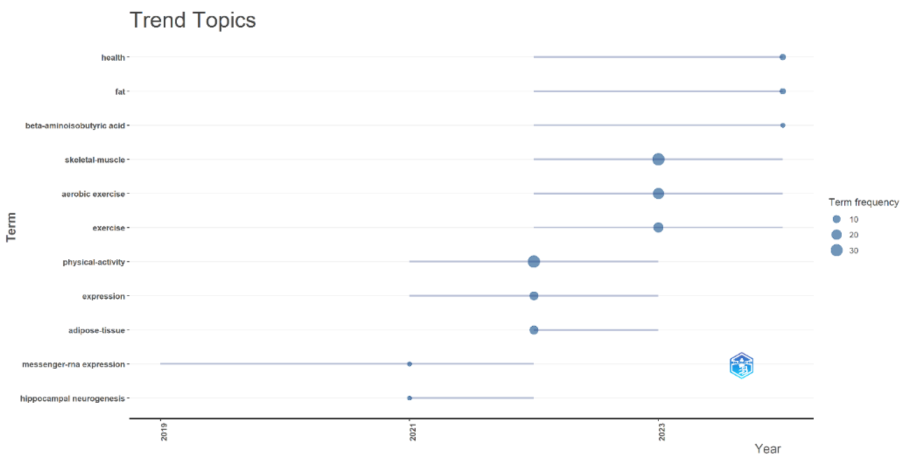

Figure 7. Trend topic analysis of keywords.

Through VOSviewer analysis, we identified a total of 833 keywords. After applying a filtering process with a minimum occurrence threshold of 5, we narrowed this down to 64 keywords. Subsequently, we created a keyword co-occurrence network map (Figure 8) that illustrates significant associations among terms such as exerkines, exercise, skeletal-muscle, myokines, neurothrophic factor, insulin-resistance, aerobic exercise and physical activity. The 64 keywords are categorized into five clusters.

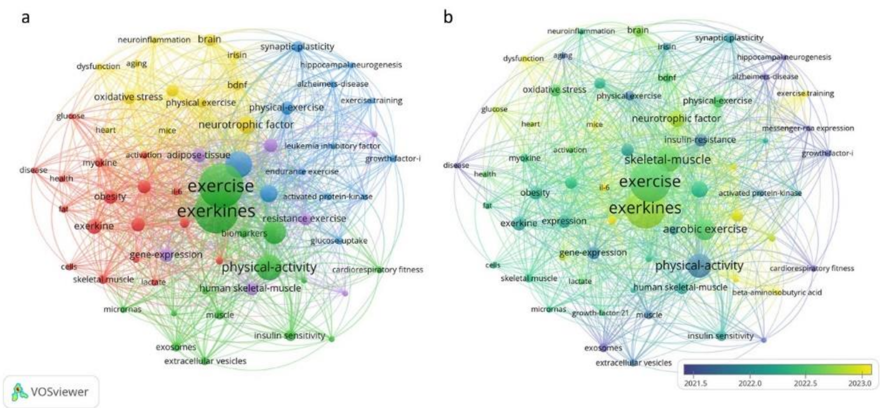

Figure 8. Co-occurrence analysis of keywords (a) Network visualization (b) Overlay visualization.

The node size shown in Figures 8a and 8b is positively correlated with the frequency of node content, and the thickness of the connection line is positively correlated with the co-occurrence times of node content at both ends. Different color clustering reflects the cooperative relationship between keywords (Figure 8a). The colors in the overlay visualization shown in Figure 8b represent the average publication year of the identified keywords. Most keywords were published after 2022, with greener colors (Figure 8b).

Discussion

Exercise is a non-pharmacological intervention that triggers the release of bioactive substances through endocrine, autocrine, and paracrine mechanisms, producing effects in various tissue systems. These bioactive substances, referred to as exerkines, encompass a wide variety of molecules, including neurotrophic factors, inflammatory mediators, myokines, hormones, adipokines, and hepatic factors (Lisa S Chow et al., 2022; Fiuza-Luces et al., 2018). These molecules may significantly play a potential role in driving the recognized benefits of exercise, such as disease prevention and management, health promotion, and enhanced resilience (Jaworska, Micielska, & Faraldi, 2024).

New evidence points to the critical role of exerkines in mediating the health benefits associated with exercise. For example, exerkines have been shown to improve cardiovascular function by reducing traditional risk factors such as obesity and hypertension while improving cardiometabolic health via mechanisms that include reduced systemic inflammation and improved vascular function (Zhou, Gong, Zhang, & Wang, 2024). Besides, myokines such as irisin and Fibroblast growth factor 21 (FGF21) have also been implicated in metabolic adaptations that enhance glucose uptake and fat oxidation, thereby reducing the risks of metabolic disorders such as type 2 diabetes (Trettel et al., 2023). Further, exerkines take part in immune system modulation. The interplay between skeletal muscle and immune responses has lately been increasingly recognized; thus, exerkines modulate lymphocyte trafficking, enhancing resilience against a myriad of diseases, including tumor conditions (Bian, Wang, Wang, & Lou, 2024).

The bibliometric analysis serves as a tool for mapping out the key areas of growth and investigation across diverse scientific domains. It helps researchers identify intersections among different fields of study, anticipate emerging trends within each discipline, and recognize significant advancements in cross-disciplinary research.

These findings align with and extend previous bibliometric analyses in exercise physiology. A recent study on exercise-regulated myokines reported a consistent upward trend in publications, with Frontiers in Physiology as the leading journal and keywords such as skeletal muscle, insulin resistance, and physical activity (Sun et al., 2024). Likewise, bibliometric reviews on irisin have identified China as the leading contributor and highlighted keywords such as exercise, obesity, and FNDC5, along with emerging interests in neuroinflammation and cognition (Gao et al., 2025). Our results mirror these patterns, with China and the United States as the top contributing countries and skeletal muscle, physical activity, and insulin resistance as the most frequent keywords. Nevertheless, unlike prior studies that focused mainly on individual molecules, the present analysis adopts a broader lens by examining exerkines as a unified field spanning multiple organ systems, thereby revealing collaborative structures and research hotspots that facilitate a more integrative understanding of exercise-induced molecular signaling.

Our bibliometric analysis shows a steady rise in research on exerkines over the last decade; however, the pace of discovery remains uneven across regions and disciplines. Notably, China and the USA dominate publication outputs, accounting for over 45% of total contributions. This concentration suggests a need for enhanced international collaboration to foster innovation and knowledge sharing in this promising field. Despite this growth, significant gaps persist in understanding the specific mechanisms of action. Future studies should prioritize investigating the dose-response relationships of different exercise modalities (e.g., comparing high-intensity interval training versus moderate-intensity continuous training) on exerkine release and their downstream effects. Additionally, research should focus on how genetic polymorphisms and environmental factors, such as nutrition, sleep quality, and stress, modulate individual exerkine responses to advance personalized exercise interventions.

Identifying key journals and prolific authors in the field provides a roadmap for future investigations into exerkines. With 87 different journals publishing on this topic, and core journals like “Frontiers in Physiology” leading the way, there is a significant opportunity for researchers to build on this knowledge base. Future studies should focus on explaining the molecular pathways through which exerkines exert their effects across various tissues and organ systems. Furthermore, it is also expected that these studies will explain how genetics, age, and other pre-existing health conditions influence exerkine responses. Ultimately, this research may enable personalized exercise prescriptions to achieve optimal health outcomes. This could further promote strategies in disease prevention and management by capitalizing on the beneficial effects of exerkines. Apart from individual variability, it is also important that researchers consider how exerkine responses are modulated by environmental factors such as dietary conditions, sleep quality, and stress intensity. These variables should, therefore, be considered in future studies to reach a comprehensive understanding of how lifestyle factors interact with physical activity at a molecular level.

The bibliometric analysis also underscores and highlights the use of interdisciplinary collaboration in forging ahead with research on exerkines. Integrating insights from fields such as molecular biology, neuroscience, nutrition science, and gerontology, for example, one can better understand how exercises at multiple levels affect health. For instance, such collaborations could develop methodological rigor and allow larger-scale studies necessary to confidently draw robust conclusions regarding the effects of exercises on diverse populations.

Limitations:

Several limitations should be acknowledged in our study. First, we retrieved publications from only one database, omitting searches in other databases such as PubMed, Scopus, Embase, or the Cochrane Library, which may have led to data omissions. Second, the extracted keywords were drawn solely from English-language articles, potentially overlooking relevant terms used in other-language publications. Third, as is inherent to bibliometric analyses, this study maps publication trends, collaborative networks, and research hotspots but does not assess the methodological quality or scientific validity of the included studies. Finally, while bibliometric analysis is a valuable supplementary tool, the findings may not fully reflect actual research conditions in the field.

Conclusion

This bibliometric analysis maps the current landscape of exerkine research, demonstrating a rapid growth in publications and identifying key themes such as skeletal muscle, physical activity, and insulin resistance. The results highlight the leading roles of China and the United States, along with influential journals and collaborative networks in this emerging field. However, these findings should be interpreted in light of the study's limitations, including the use of a single database and restriction to English-language publications. Although the field shows promising development, significant gaps persist in understanding the underlying mechanisms and clinical applications of exerkines. Future studies should prioritize interdisciplinary collaboration to translate these bibliometric insights into targeted research on exercise prescriptions and therapeutic interventions aimed at improving metabolic health and disease prevention.

Author Contributions:

HP: Wrote the Manuscript, Conceptualization, Formal Analysis, Investigation, Methodology, Project Administration, Writing–review and editing; **BK:** Supervision, Writing–review and editing; **BT:** Supervision, Writing–review and editing; **RE:** Conceptualization, Investigation, Supervision, Writing–review and editing; **MR:** Critically Reviewed the Manuscript.

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