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Research Collaboration and Trends on Bioactive Compounds and Pharmacological Activities of Black Rice Bran: A Bibliometric Analysis

I Gusti Yogaswara[1], Lalu Husnul Hidayat[1], Navista Sri Octa Ujiantari[2], Soni Siswanto[3*]

[1] Master in Pharmaceutical Sciences Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia.
[2] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia.
[3] Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia.

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Corresponding Author:
Soni Siswanto
soni.siswanto@ugm.ac.id

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Abstract: Black rice bran is an agricultural by-product rich in secondary metabolites with potential pharmacological activities, particularly antioxidant and antidiabetic effects. Despite increasing research on its bioactive compounds, the development of research trends and collaboration patterns in this field has not been systematically analyzed. This study aims to evaluate global research trends on the secondary metabolites and pharmacological activities of black rice bran using a bibliometric approach. Bibliographic data were retrieved from the Scopus database and selected using the PRISMA 2020 framework. The dataset was cleaned using OpenRefine and analyzed using the Bibliometrix R-package via the Biblioshiny interface, while network visualization was performed using VOSviewer. The results show a gradual increase in publications, particularly after 2018, with research mainly published in journals related to food chemistry and functional foods. Institutional contributions are largely dominated by Southeast Asian universities, especially in Thailand. Thematic evolution indicates a shift from phytochemical characterization toward pharmacological investigations, particularly antioxidant and antidiabetic activities. These findings highlight the growing scientific interest and potential of black rice bran as a promising natural resource for health promotion.

Keywords: Bibliometric analysis; Black rice bran; Diabetes; Inflammation; Secondary metabolites

Introduction

Rice (*Oryza sativa* L.) is a staple food for more than half of the world's population. Before consumption, rice grains undergo milling, which produces rice bran as a by-product rich in bioactive compounds. These compounds are predominantly concentrated in the bran layer, including the pericarp, aleurone layer, and seed coat, whereas the inner endosperm contains significantly lower levels of phytochemicals. Rice bran is known to contain various secondary metabolites such as anthocyanins, phenolic acids, flavonoids, tocopherols, tocotrienols, and γ-oryzanol, which contribute to antioxidant, antimicrobial, antidiabetic, and hypolipidemic activities (Andriani et al., 2022; Spaggiari et al., 2021; Tan et al., 2023; Verma & Srivastav, 2020; Wang et al., 2018; Zarei et al., 2017). In black rice, approximately 97% of the total anthocyanin content is located in the bran, giving the outer layer its characteristic deep purple to black pigmentation due to the high accumulation of anthocyanins (Mackon et al., 2021). Despite its rich phytochemical composition, rice bran remains underutilized in the human food chain, even though it has considerable potential as a source of functional food ingredients and nutraceutical compounds (Andriani et al., 2022; Tan et al., 2023).

Among pigmented rice varieties, black rice bran has consistently been reported to possess higher

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phytochemical content and stronger antioxidant capacity compared with red and brown rice bran, as well as greater antiproliferative activity against cancer cells (Ghasemzadeh et al., 2018; Yuliana et al., 2020). Various phytochemical and metabolomic studies have identified numerous bioactive compounds in black rice bran, including phenolic acids such as protocatechuic acid, ferulic acid, and gallic acid, as well as flavonoids that exhibit multiple pharmacological activities. These compounds have been reported to act as cytotoxic agents, apoptosis inducers, and inhibitors of α-glucosidase activity, indicating potential roles in anticancer and antidiabetic therapies (Bhuyan et al., 2022; Ghasemzadeh et al., 2018; Teethaisong et al., 2025; Yuliana et al., 2020; Zarei et al., 2017). In addition, experimental studies have demonstrated gastroprotective effects, in vivo antioxidant activity, and a favorable acute toxicity profile of black rice bran extracts in animal models, further supporting their potential application in functional foods and nutraceutical products (Tonchaiyaphum et al., 2021).

Research on rice bran bioactive compounds has grown significantly in recent years due to the growing interest in the sustainable use of agricultural by-products and the development of functional foods. Through narrative reviews or limited bibliographic analyses, a number of research have attempted to analyze the composition and health-related activities of rice bran (Kumar et al., 2023; Ooi et al., 2023). However, these studies generally focus on rice bran in general and do not specifically examine the global research landscape related to secondary metabolites of black rice bran and their pharmacological activities.

The rapid growth of scientific publications in this field highlights the importance of bibliometric analysis as a systematic approach to evaluate research development, identify major themes, and uncover collaboration patterns and knowledge gaps. Although several bibliometric studies have examined rice bran research, comprehensive mapping specifically focused on the secondary metabolites and pharmacological activities of black rice bran remains limited. Therefore, this study analyzes global research trends related to the secondary metabolites and pharmacological activities of black rice bran using a bibliometric approach. The analysis explores publication growth, collaboration networks, major research themes, and keyword evolution to provide a comprehensive overview of the research landscape. In addition, this study identifies emerging directions and research gaps that may support future investigations and promote the utilization of black rice bran bioactive compounds for health promotion, disease prevention, and potential therapeutic development.

Method

This study employed a bibliometric analysis approach to evaluate global research trends related to secondary metabolites and pharmacological activities of black rice bran. Bibliographic data were retrieved from the Scopus database (www.scopus.com) on 07 February 2026 to ensure transparency and reproducibility of the dataset. Scopus was selected as the primary data source because it is widely recognized as a reputable indexing database that provides accurate and comprehensive bibliographic information, including publication metrics, citations, authorship, and journal quality indicators (Evendi, 2022). The bibliometric analysis method was conducted in stages using Scopus data with the keywords (*("black rice bran" OR "black rice" OR "Oryza Sativa") AND ("secondary metabolites" OR "bioactive compounds" OR "phytochemicals" OR "metabolites") AND ("pharmacological activity" OR "biological activity" OR "therapeutic effects" OR "health benefits")).* Only documents written in English and published between 1992 and 2025 were included. The document selection process followed the PRISMA 2020 framework (Page et al., 2021), which can be seen in Figure 1. The process of identification, screening, eligibility assessment, and inclusion of studies was documented following the PRISMA 2020 flow to ensure transparency and replication of document selection (Tofigh et al., 2025).

The retrieved records were exported in CSV format and subsequently cleaned by removing duplicates and irrelevant entries using OpenRefine (Ham, 2013). The curated dataset was then analyzed using the Bibliometrix R-package via the Biblioshiny web interface (Aria & Cuccurullo, 2017), while network visualization was performed using VOSviewer (Van Eck & Waltman, 2010). VOSviewer is widely used in bibliometric studies due to its ability to process datasets from various databases, including Scopus and Web of Science, and to visualize bibliometric networks such as author collaboration, keyword co-occurrence, and co-citation relationships (Nurvianie & Sundari, 2024; Safitri & Admoko, 2024). Meanwhile, Bibliometrix was applied to analyze publication trends, leading journals and major contributing institutions (Pananrangi, 2025). These procedures are commonly employed in Scopus-based bibliometric studies (Kamaruzzaman et al., 2022).

The bibliometric analysis consisted of several analytical components. First, descriptive analysis was conducted to examine annual scientific production, most productive authors, and most relevant journals. Second, source analysis was performed using Bradford's Law to identify core journals in the field. Third, the conceptual structure of the research field was analyzed using keyword co-occurrence networks and thematic mapping

to identify dominant research themes. Finally, the social structure of the research field was examined through co-authorship network analysis to explore collaboration patterns among researchers and countries (Klarin, 2024).

Network visualization included keyword co-occurrence, co-authorship, and citation networks, producing both network visualization maps and density maps in accordance with recommended bibliometric practices (Al Husaeni & Nandiyanto, 2021; Cagorol & Sarsale, 2025). For network construction, a minimum threshold of 5 keyword occurrences and 2 documents per author was applied to ensure clarity and interpretability of the visualization. The resulting visual outputs, including trend graphs, thematic maps, and collaboration networks, were interpreted to identify research trends, dominant themes, research gaps, and key contributors in the field.

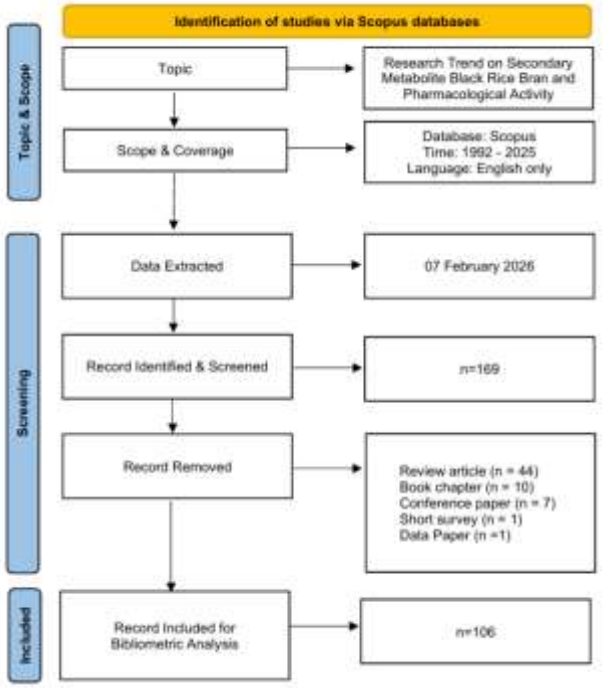


Figure 1. Flow diagram of the search strategy

Result and Discussion

Annual Scientific Production

Based on Figure 2 (a), which illustrates the annual scientific production retrieved from the Scopus database, the number of publications related to black rice bran secondary metabolites and pharmacological activities shows a fluctuating but generally increasing trend during the period 1992–2025. At the beginning of the observation period in 1992, only one publication was recorded, followed by a relatively low publication frequency until the early 2000s. From 2001 to 2006, the number of publications gradually increased, although several years still showed limited research output. Between 2007 and 2018, the publication trend continued to fluctuate but with a higher frequency, ranging from three to seven publications per year. A more noticeable increase occurred after 2019, indicating growing scientific interest in the pharmacological potential and bioactive compounds of black rice bran. In total, 64 publications were produced between 2019 and 2025, reflecting the recent expansion of research in this field. However, it should be noted that the data for 2025 may still represent partial indexing in the Scopus database, as the dataset was retrieved on 07 February 2025. The observed growth in publication output may be associated with increasing research attention toward functional foods, nutraceutical development, and the pharmacological potential of plant-derived bioactive compounds. The growth in the number of publications can be attributed to the increasing interest of researchers in developing topics. In addition, the increase in the number of publications proves the urgency of this theme felt by researchers (Rambe et al., 2025).

Sources' Production over Time

The analysis of sources' production over time (Figure 2 (b)) illustrates the temporal contribution of several major journals publishing research related to black rice bran secondary metabolites and pharmacological activities. The cumulative trend indicates that publications began to appear more consistently after 2006, with a noticeable increase in growth after 2016. The Journal of Agricultural and Food Chemistry was among the earliest journals publishing studies on this topic, with contributions recorded in 2006, indicating its early role as a publication venue for research on the chemical composition and bioactive compounds of black rice bran.

Meanwhile, Food Research International began contributing publications in 2011 and showed a steady cumulative increase until 2025. Other journals, including Cereal Chemistry, Journal of Food Measurement and Characterization, and LWT, began contributing later, mainly between 2016 and 2018. This pattern suggests that research on black rice bran has gradually expanded into broader areas such as food quality evaluation, compound characterization, and functional food development.

The simultaneous increase in publications across several journals after 2018 indicates a phase of accelerated research activity in this field. However, the distribution of publications across multiple journals suggests that the research domain remains relatively dispersed rather than dominated by a single journal. Most of the contributing journals are primarily focused on food science and agricultural chemistry, reflecting the current emphasis on compositional analysis and

functional food applications. This pattern also indicates that research on the pharmacological and therapeutic aspects of black rice bran is still developing compared with studies focused on food chemistry and bioactive compound characterization.

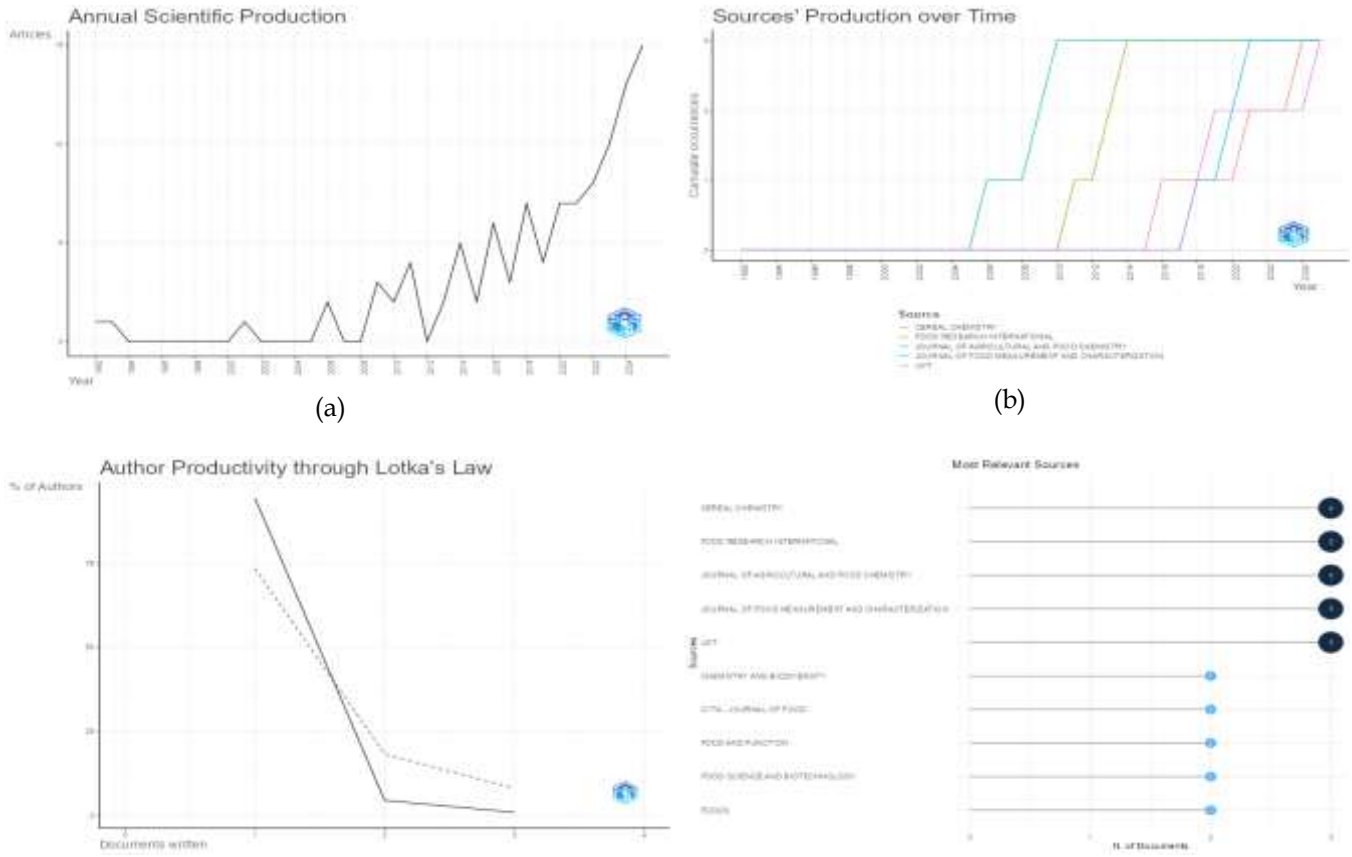


Figure 2. (a) Annual scientific production from 1992—2025, (b) Visualization of sources' production over time, (c) Authors' productivity in accordance with Lotka's Law, (d) Visualization of the most relevant sources on black rice bran secondary metabolites and pharmacological activity publishing research

Author Productivity through Lotka's Law

The distribution of author productivity follows the pattern described in Lotka's Law, which states that most authors contribute to only one article, while a small proportion of authors have more than one publication (Bidwe & Waghmare, 2024). Figure 2 (c) and table 1 show that a high proportion of authors, approximately 94% of authors contributed only a single publication within the dataset. This pattern indicates that research on black rice bran secondary metabolites and pharmacological activities is conducted by many authors with limited individual publication frequency, while only a few researchers contribute repeatedly to the field. Such a distribution is commonly observed in emerging or interdisciplinary research areas, where contributions come from diverse research groups rather than a small number of highly specialized authors. This finding suggests that the research domain is still developing and that sustained contributions from leading authors may help strengthen collaboration networks and thematic specialization in the future.

Table 1. Author Productivity as per Lotka's Law on Black Rice Bran Secondary Metabolites and Pharmacological Activity

Documents written	N. of Authors	Proportion of Authors	Theoretical
1	557	0.94	0.73
2	27	0.04	0.18
3	6	0.01	0.08

Most Relevant Sources

Based on an analysis of scientific publications on the topic of "Black Rice Bran Secondary Metabolites and Pharmacological Activity", there are 81 journal names that serve as publication media with varying numbers of scientific publications. The distribution of scientific publications forms a pattern that indicates that some journals have a more dominant contribution, while others may be evenly distributed or relatively few

(Rannisa et al., 2025). Figure 2 (d) shows the top 10 journals with the highest number of publications. There are several journals with the same number of scientific publications, each having three publications: Cereal Chemistry, Food Research International, Journal of Agricultural and Food Chemistry, Journal of Food Measurement and Characterization, and LWT. This finding suggests that these 5 journals are among the more frequently utilized outlets for disseminating research on black rice bran secondary metabolites and pharmacological activity, though the relatively low number of publications (3 each) indicates that no single journal dominates the field yet. In addition, the number of 2 scientific publications in each journal was occupied by the journals Chemistry and Biodiversity, CYTA - Journal of Food, Food and Function, Food Science and Biotechnology, and Foods.

From these results, a pattern emerges of relatively even distribution across multiple journals, with no overwhelming concentration in any one outlet. To understand this, we examined the scopes of the top journals. For instance, the five journals with three publications each. Cereal Chemistry, Food Research International, Journal of Agricultural and Food Chemistry, Journal of Food Measurement and Characterization, and LWT, primarily focus on food chemistry, grain processing, nutraceuticals, and analytical characterization of bioactive compounds. This alignment explains why research on black rice bran, rich in secondary metabolites like anthocyanins with potential pharmacological activities (e.g., antioxidant and inflammation effects), is frequently submitted here: these journals emphasize the intersection of agriculture, food science, and health benefits.

Similarly, journals with two publications, such as Chemistry and Biodiversity (focused on natural product diversity and bioactivity), CYTA - Journal of Food (emphasizing food technology and nutrition), Food and Function (linking food components to physiological effects), Food Science and Biotechnology (covering biotechnological applications in foods), and Foods (broad food science including functional ingredients), reflect a pattern where black rice bran studies are drawn to outlets that bridge chemistry, biotechnology, and pharmacology. This distribution highlights the interdisciplinary nature of the topic, involving fields like chemistry, functional foods, agriculture, biology, pharmacy, and biotechnology. Overall, the pattern suggests that publications target journals specializing in functional foods and pharmaceutical applications of plant-derived compounds, underscoring black rice bran's potential in health-related research despite the modest publication volumes per journal.

In contrast, most of the other journals (71 titles) each published only one article, contributing to a broad but diffuse distribution. This widespread, combined with the low maximum of three publications per journal, indicates an emerging field without established 'core' journals, rather than a mature one with dominant targets

Three-Field Plot

Figure 3 presents a three-field plot connecting title terms (TI_TM), authors (AU), and author keywords (DE) in studies related to the secondary metabolites and pharmacological activities of black rice bran. This visualization demonstrates the relationships between frequently used title terms, the contributing authors, and the keywords that represent the main research themes. The thickness of the connecting lines reflects the strength of the relationships among these elements.

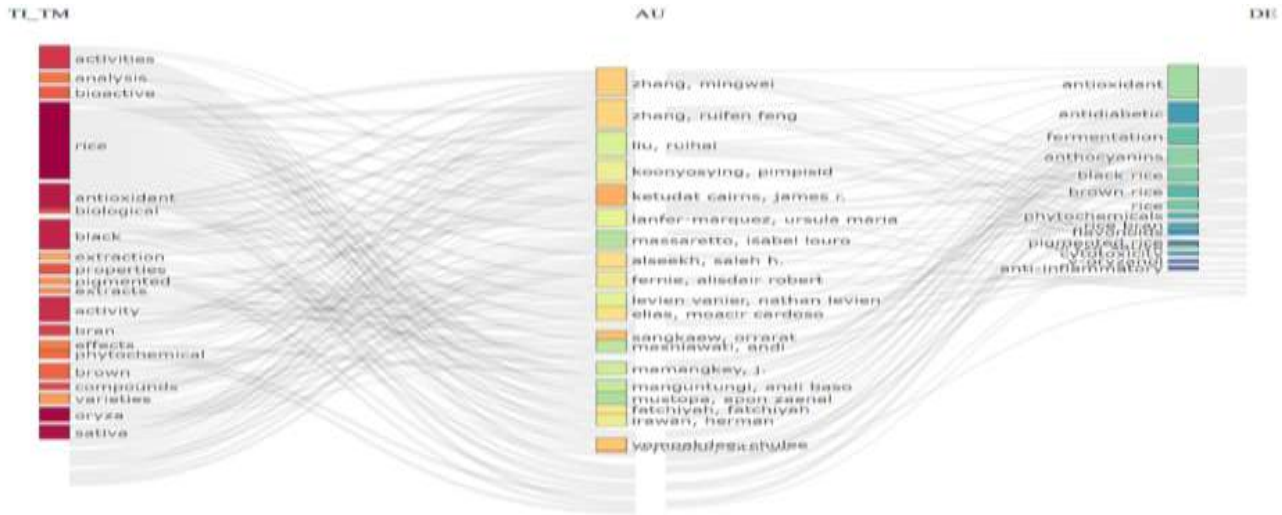
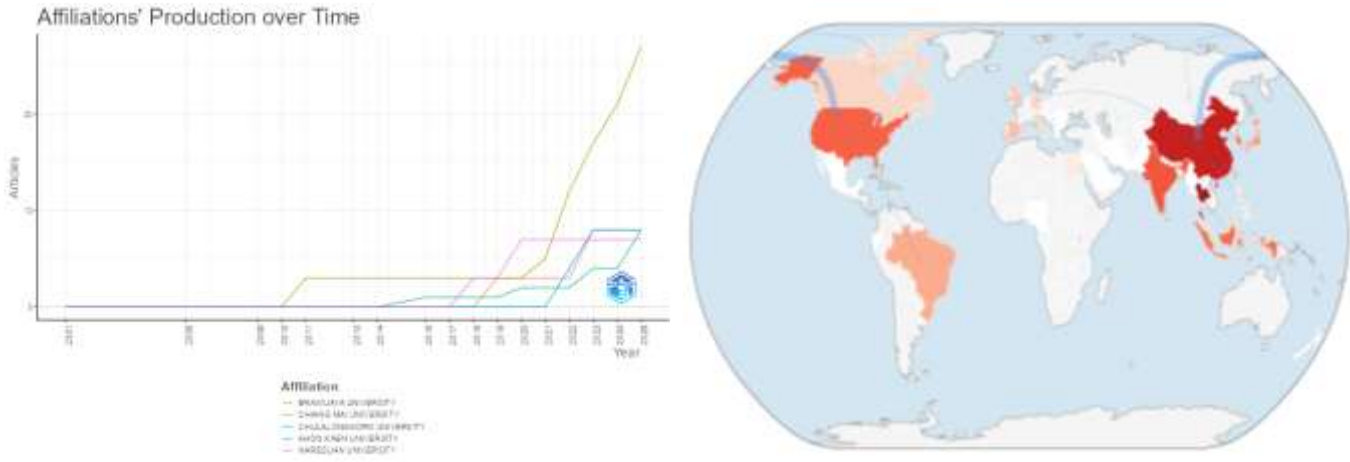


Figure 3. Three-field plot map showing the relationship between authors (AU), titles (TI_TM), and keywords (DE) of research publications on black rice bran secondary metabolites and pharmacological activity



(a) (b)

Figure 4. (a) Affiliations' production-wise trends publishing research, (b) Visualization of countries' collaboration world map on black rice bran secondary metabolites and pharmacological activity

The most frequently occurring title terms include "rice," "antioxidant," "black," "activity," and "phytochemical," indicating that many studies primarily focus on the bioactive compounds and biological activities associated with rice. Several researchers, including Zhang Mingwei, Zhang Ruifen Feng, Liu Ruihai, Ketudat Cairns James R., and Mamangkey J., are connected to multiple title terms and keywords, suggesting their significant contributions and active involvement in this research area. Regarding the keyword field, frequently appearing terms include "antioxidant," "antidiabetic," "anthocyanins," "black rice," and "phytochemicals." These keywords represent the dominant research themes, particularly studies examining the antioxidant and antidiabetic potential of anthocyanin-rich black rice bran. Overall, the three-field plot highlights the close relationship between research on rice-derived bioactive compounds and their pharmacological activities, reflecting the increasing scientific interest in the functional and therapeutic potential of black rice bran.

Core Sources by Bradford's Law

Bradford's Law was applied to identify the core journals contributing to research on black rice bran secondary metabolites and pharmacological activities. According to Bradford's distribution, journals are divided into several zones based on their productivity, where a small number of journals typically contribute a large proportion of articles in a specific research field (Naorem et al., 2024).

Table 2. Core Sources as per Bradford's Law in Publishing Research on Black Rice Bran Secondary Metabolites and Pharmacological Activity

SO	Rank	Freq	cumFreq	Zone
Cereal chemistry	1	3	3	Zone 1
Food research international	2	3	6	Zone 1
Journal of agricultural and food chemistry	3	3	9	Zone 1
Journal of food measurement and characterization	4	3	12	Zone 1
LWT	5	3	15	Zone 1
Chemistry and biodiversity	6	2	17	Zone 1
CYTA - Journal of food	7	2	19	Zone 1
Food and function	8	2	21	Zone 1
Food science and biotechnology	9	2	23	Zone 1
Foods	10	2	25	Zone 1

Based on table 2, the journals with the highest number of publications include Cereal Chemistry, Food Research International, Journal of Agricultural and Food Chemistry, Journal of Food Measurement and Characterization, and LWT, each contributing three articles. Several other journals, including Chemistry and Biodiversity, CYTA – Journal of Food, Food and Function, Food Science and Biotechnology, and Foods, each contributed two articles. However, the relatively small number of publications per journal and the presence of many journals publishing only one article indicate that the research output is widely dispersed across different sources. This pattern suggests that the research field remains relatively fragmented and has not

yet developed a strongly defined core journal structure. Most contributing journals belong to the fields of food science, agricultural chemistry, and functional foods, reflecting the interdisciplinary nature of research on black rice bran bioactive compounds.

Affiliations' Production over Time

Affiliations' production over time analysis is used to examine article production based on affiliations over time in relation to colleges or universities (Safitri & Ramadhan, 2023). The Figure 4 (a) shows that several universities from Thailand appear as major contributors to research on black rice bran secondary metabolites and pharmacological activity.

Specifically, Chiang Mai University demonstrates the most consistent publication growth, with research output gradually increasing since around 2011 and reaching the highest cumulative number of publications by 2025. Naresuan University shows a noticeable increase in publication activity during the 2018–2020 period, followed by a relatively stable trend in subsequent years. Meanwhile, Khon Kaen University exhibits a slower growth pattern before experiencing an increase in publication output starting in 2022. Chulalongkorn University contributes publications intermittently over time, indicating moderate research activity. In addition, Brawijaya University began contributing to this research area around 2018, with gradual growth in publications until 2023–2024.

Overall, these trends indicate that research output in this field is supported by several active institutions, particularly universities in Southeast Asia, which contribute continuously to the development of studies on black rice bran and its pharmacological potential.

Countries' Collaboration World Map

The countries' collaboration map in figure 4 (b) shows the dominance of Asian countries, particularly China, the Philippines, and Thailand. This dominance is understandable given that black rice is a commodity that is widely cultivated in Asia. This can be seen from the dark red color indicating strengthened partnerships. Meanwhile, cross-continental collaboration is still relatively limited. Increased international cooperation has the potential to broaden the research approach. This increases the opportunities for collaboration between countries from different continents.

Most Relevant Authors

Figure 5 presents the most relevant authors contributing to research on black rice bran secondary metabolites and pharmacological activity. The results show that publication contributions in this field are relatively dispersed and not dominated by a single research group. Based on the number of articles, Ketudat Cairns, James R.; Roytrakul, Sittiruk; Sangkaew, Orrarat; Yompakdee, Chulee; Zhang, Mingwei; and Zhang, Ruifen Feng each have three publications in the dataset.

In addition to total publications, the analysis also considers fractionalized articles, which reflect the proportional contribution of authors within collaborative publications. Roytrakul, Sangkaew, and Yompakdee show relatively higher fractional values (approximately 0.64), indicating a greater proportional contribution in their publications, while some authors with similar publication counts have lower fractional values due to broader collaboration networks. Other authors, such as Alseekh, Saleh H.; Elias, Moacir Cardoso; and Fatchiyah, Fatchiyah, contributed two publications with varying levels of contribution. The difference between the total number of articles and the fractional value reflects the dynamics of collaboration in this field. A higher fractional value indicates a major authorship role, while a lower value indicates involvement in a larger collaboration network (Sailendra Malik, 2025).

Overall, the absence of a highly dominant author suggests that research on black rice bran secondary metabolites and pharmacological activity is still developing and distributed across multiple research groups, reflecting the interdisciplinary nature of this field, particularly in food chemistry, biochemistry, and health sciences.

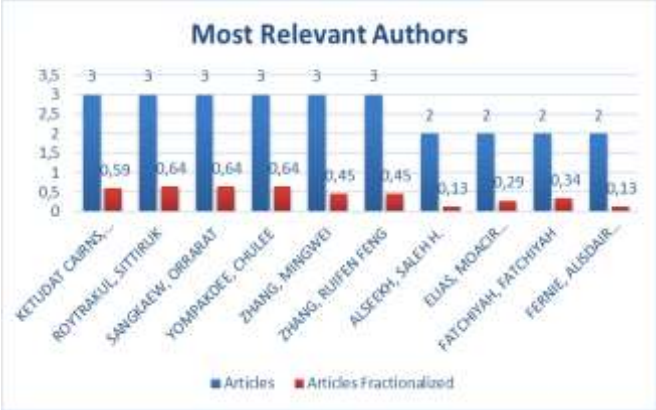


Figure 5. Visualization of most relevant authors publishing research on black rice bran secondary metabolites and pharmacological activity

Trend of Topics

The analysis of topic trends (Figure 6) illustrates the evolution of research themes over time. In this visualization, the horizontal axis represents the publication year, while the vertical axis lists the main research terms, and the size of each circle indicates the frequency of term occurrence in the literature (Susanti & Desa, 2026; Utami et al., 2025). In the early phase, research focused more on bioactive compounds, total phenolics, and functional foods. These themes reflect the

initial emphasis on the chemical characterization of black rice bran and its potential as a functional food ingredient.

The 2017–2021 period was marked by an increase in the frequency of the term's anthocyanins, antioxidants, and black rice. This confirms that black rice, especially black rice bran, contains bioactive compounds that help reduce the risk of various diseases and improve health (Rukmana et al., 2025). The presence of anthocyanins (cyanidine-3-glucoside) in the bran layer of black rice makes it a good source of antioxidants (Das et al., 2023).

In the recent period (2023–2025), the keyword "antidiabetic" has emerged, indicating a shift in research focus toward therapeutic applications, particularly in metabolic disorders. This trend suggests that recent studies increasingly aim to validate the pharmacological potential of bioactive compounds found in black rice bran.(Eviana et al., 2023). Overall, the evolution of these topics demonstrates a progression of research from chemical characterization toward pharmacological investigation and potential health-related applications.

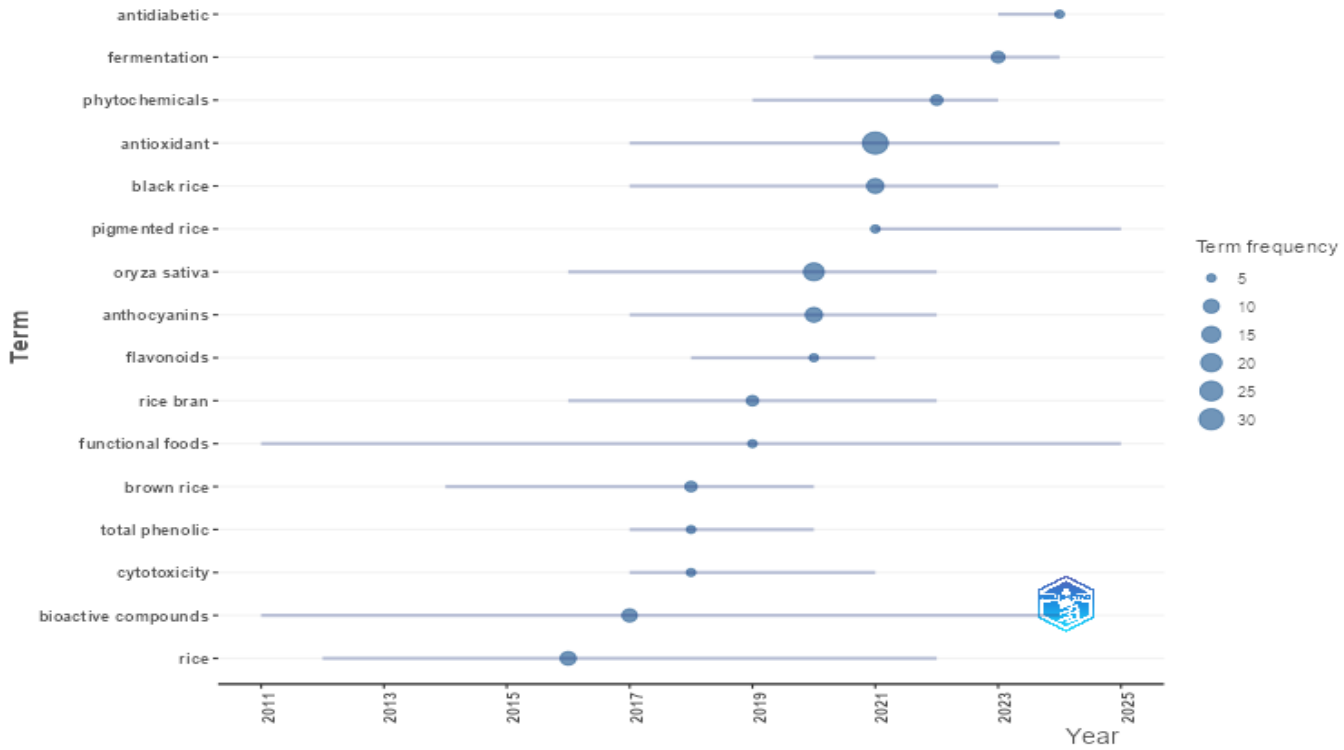


Figure 6. Visualization trend of topic publishing research on black rice bran secondary metabolites and pharmacological activity

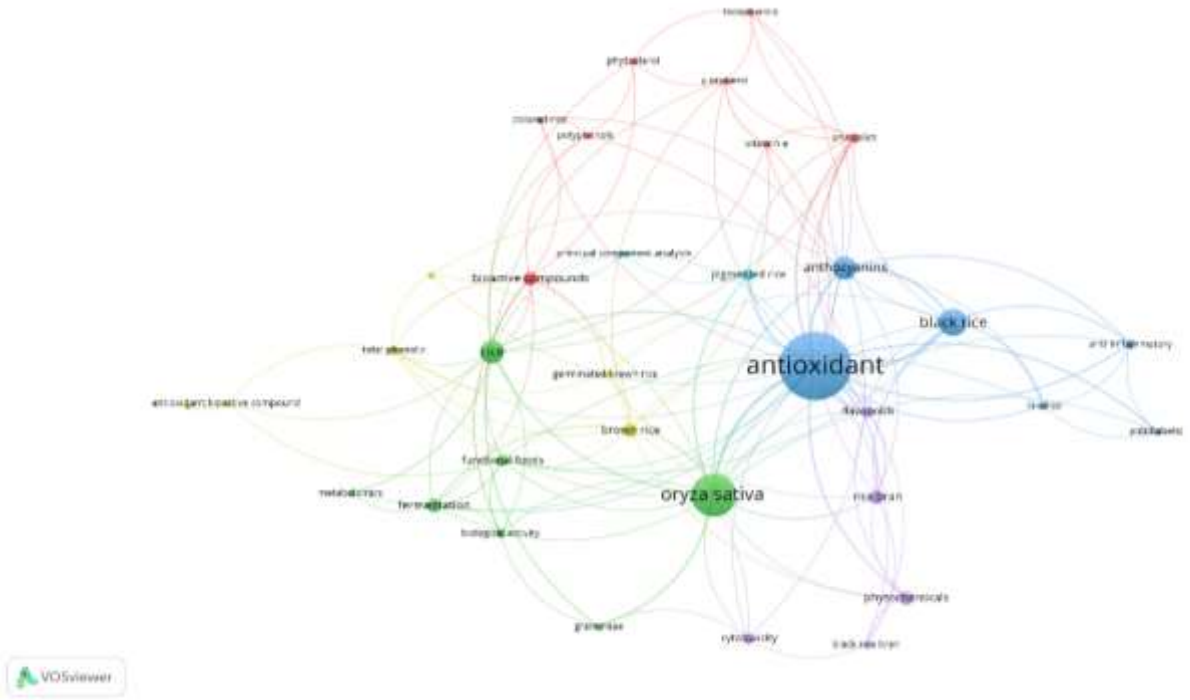
Co-occurrence Network

Co-occurrence analysis was conducted to identify relationships among research concepts and detect dominant and emerging themes in the field (Ananda et al., 2024; Husni et al., 2025; Simarmata & Fathurrahman, 2025). The bibliometric mapping was visualized using VOSviewer, which allows the display of bibliometric networks in several forms such as network and overlay visualization (Fitri et al., 2023).

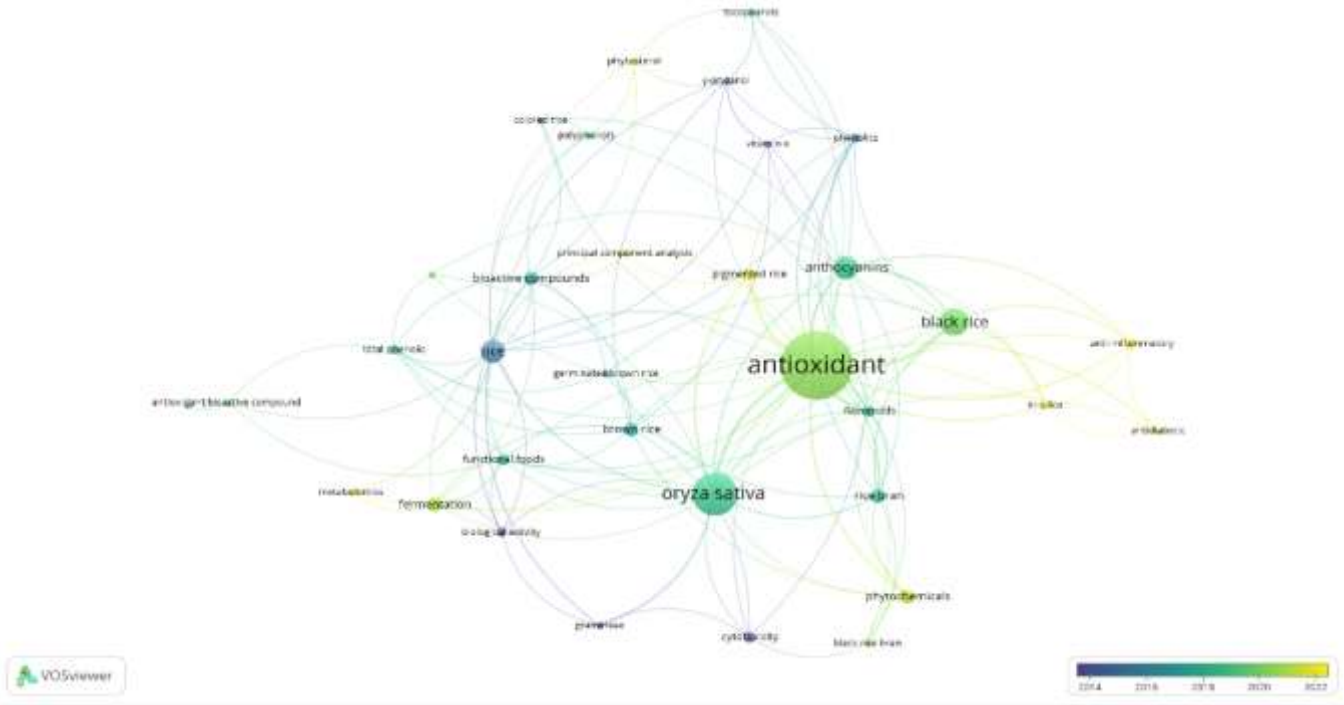
Figure 7 (a) shows the visualization of co-occurrence networks generated using VOSviewer, revealing three main clusters. The first cluster centers on antioxidants with dominant pharmacological activity, which have been linked to other biological activities such as antidiabetic and antiinflammatory effects. The second cluster relates to Oryza sativa, which shows a strong association with its use as a functional food and its recognized biological activities. The bioactive compounds in black rice bran are considered superfoods that play an important role in promoting health (Estiasih et al., 2021). The third cluster is associated with the phytochemical content of black rice bran. Previous studies report that black rice bran exhibits several biological activities, including cytotoxic, antidiabetic, antiinflammatory, and antioxidant properties, highlighting its potential for the development of natural-based therapeutic agents in the era of increasing degenerative diseases (Mapoung et al., 2023; Monikasari et al., 2023).

Figure 7 (b) presents the overlay visualization showing the temporal development of research topics. Recent studies increasingly associate antioxidant activity with other pharmacological activities, particularly antidiabetic effects. This trend indicates a

growing research focus on metabolic and inflammatory diseases, especially diabetes and inflammation-related disorders. The increasing attention to these topics suggests that bioactive compounds in black rice bran, such as anthocyanins and phenolic compounds, are being increasingly explored for their potential roles in the prevention and management of chronic diseases. Overall, this pattern demonstrates that current research trends are shifting from basic phytochemical identification toward the investigation of biological activities and potential health applications of black rice bran.



(a)



(b)

Figure 7. Visualization of co-occurrence (a) network visualization (b) overlay visualization, publishing research on black rice bran secondary metabolites and pharmacological activity

Conclusion

This bibliometric study provides a comprehensive overview of global research trends on the secondary metabolites and pharmacological activities of black rice bran. The results indicate a gradual increase in scientific publications, reflecting growing interest in the health potential of this agricultural by-product. Author productivity analysis shows that most contributors are transient authors, suggesting that a specialized research community in this field is still emerging. Institutional contributions are dominated by Southeast Asian universities, particularly in Thailand, while publications are mainly distributed across journals focusing on food chemistry and functional foods. Thematic evolution demonstrates a shift from early phytochemical characterization toward investigations of pharmacological activities, especially antioxidant, antiinflammation and antidiabetic properties. Future research should emphasize interdisciplinary collaboration and further explore pharmacological validation to support the development of black rice bran as a promising natural resource for health promotion and therapeutic applications.

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Author Contributions
Conceptualization, S.S., I.G.Y; methodology, S.S., I.G.Y and L.H.H.; formal analysis, I.G.Y. and S.S.; investigation, I.G.Y.; data curation, I.G.Y.; visualization, I.G.Y. and H.H.; validation, N.S.O.U.; writing—preparation of original draft, I.G.Y.; writing—reviewing and editing, S.S. and N.S.O.U.; supervision, S.S. and N.S.O.U.; data analysis, H.H. All authors have read and approved the published version of the manuscript.

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Conflicts of Interest
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