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Global Knowledge Structure and Research Fronts of Kaempferol in Antidiabetic Studies: A Bibliometric and Science Mapping Analysis

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ABSTRACT

Kaempferol, a widely distributed natural flavonoid, is increasingly studied for its antidiabetic properties. However, a comprehensive bibliometric analysis mapping the global research landscape of this field is currently lacking. This study aims to map research trends, collaborations, and the thematic evolution of kaempferol in diabetes-related studies from 2000 to 2025, while identifying emerging hotspots such as nutrigenomics and metabolomics. A total of 700 scientific documents were retrieved from the Scopus database. Bibliometric indicators and science mapping techniques—utilizing VOSviewer and Biblioshiny (RStudio)—were employed to analyze keyword co-occurrence networks, thematic evolution, and research dynamics. The field demonstrated a 19.5% average annual growth rate, encompassing 265 journals and 4,089 authors, reflecting a highly collaborative global environment. Thematic evolution revealed a distinct shift from early foundational studies on antioxidant activity and enzyme inhibition toward current research emphasizing molecular docking, gene modulation, and metabolic profiling. Recently, nutrigenomics and metabolomics have emerged as prominent focus areas. This bibliometric analysis provides a quantitative overview of the research landscape surrounding kaempferol and diabetes. The findings highlight an ongoing transition toward integrative, omics-based strategies, offering a structured foundation to guide future mechanistic and translational investigations.

Key Messages:

- Bibliometric evidence reveals a rapidly expanding research landscape for kaempferol in diabetes, marked by a distinct thematic shift from basic antioxidant studies toward advanced, omics-based approaches such as nutrigenomics and metabolomics.

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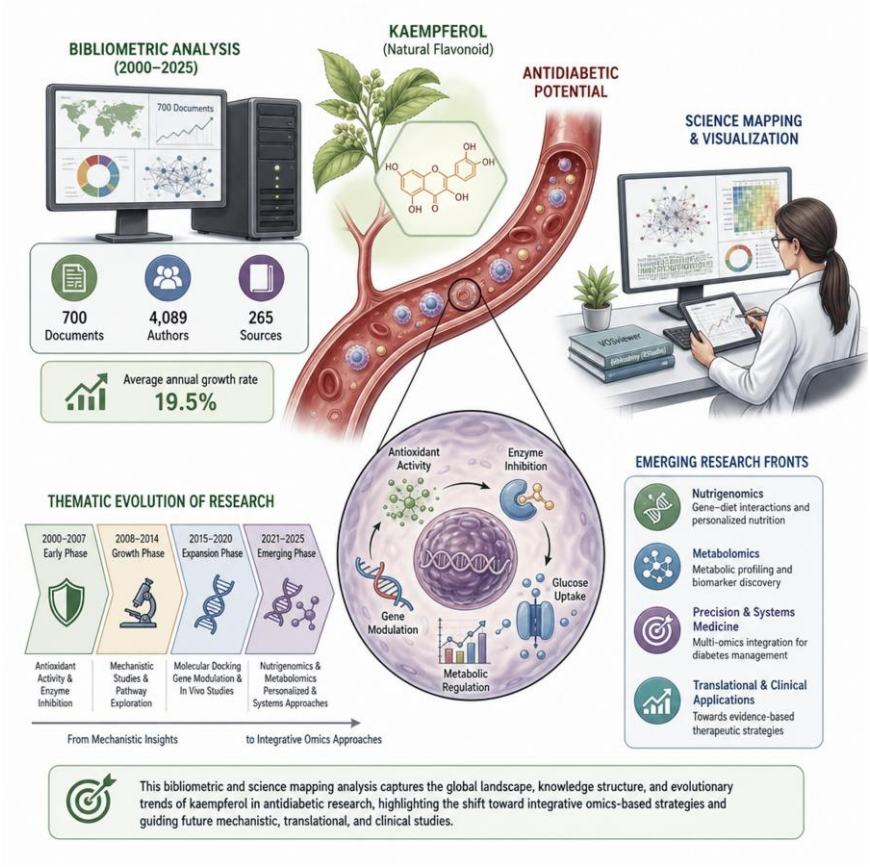
GRAPHICAL ABSTRACT



INTRODUCTION

Type 2 diabetes mellitus (T2DM) has emerged as one of the most critical global health challenges, representing a major global health challenge and imposing a substantial socioeconomic burden worldwide (1). The pathophysiology of T2DM involves a multifaceted interplay of insulin resistance, impaired insulin secretion, and pancreatic β-cell dysfunction, conditions often exacerbated by genetic predisposition, sedentary lifestyle, and comorbid metabolic disorders such as obesity and dyslipidemia (2,3). Despite advances in pharmacotherapy, major challenges persist, including adverse long-term effects, declining efficacy over time, and the unmet need for more personalized therapeutic strategies (4).

These challenges have stimulated growing scientific interest in nutraceuticals and plant-derived bioactive compounds as safer, affordable, and potentially synergistic alternatives or complements to conventional therapy (5–8). Among these, flavonoids stand out due to their well-documented anti-inflammatory, antioxidant, and metabolic regulatory activities that align closely with the underlying mechanisms of diabetes pathophysiology (9–11).

Among thousands of flavonoids identified in nature, kaempferol (3,5,7-trihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one) has received increasing scientific attention (12). This aglycone compound is abundant in common dietary sources such as tea, broccoli, kale, and grapes, contributing to many of the health-promoting effects attributed to these foods (13,14). A growing body of preclinical evidence supports kaempferol's antidiabetic potential through multiple cellular and molecular mechanisms (15–17).

Mechanistically, kaempferol exerts diverse actions that collectively modulate glucose homeostasis. First, it enhances insulin sensitivity by promoting glucose uptake in muscle cells and adipocytes (18–20). Second, it inhibits hepatic gluconeogenesis by suppressing key enzymes such as pyruvate carboxylase (21,22). Third, kaempferol acts as a potent antioxidant and anti-inflammatory agent, mitigating oxidative stress and downregulating pro-inflammatory cytokines (e.g., TNF-α, IL-6), thereby protecting pancreatic β-cells from damage a critical factor in the progression of T2DM (15). Additionally, kaempferol and its

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glycosides demonstrate inhibitory activity against α-glucosidase and α-amylase, effectively modulating postprandial hyperglycemia (23). These actions underscore kaempferol's dual role as both a pharmacologically active compound and a nutritional bioeffector, positioning it as a promising candidate for translational nutraceutical development.

Despite extensive molecular studies, however, current research on kaempferol remains largely reductionist, focusing on isolated biochemical pathways or single-target mechanisms. A substantial knowledge gap persists regarding its integrated action within the complex biological network of human metabolism. Specifically, the incorporation of omics-based approaches including genomics, proteomics, transcriptomics, and metabolomics remains limited (24,25). Two major underexplored dimensions are evident: 1) nutrigenomics, which could reveal how kaempferol modulates gene expression and epigenetic regulation linked to glucose and lipid metabolism, and 2) metabolomics, which could uncover global metabolic changes associated with kaempferol exposure in diabetic systems (26–28).

Given the exponential rise in publications investigating kaempferol's therapeutic potential, there is an urgent need to systematically organize and quantify the evolving knowledge landscape. Bibliometric and science mapping analysis provide powerful quantitative tools to visualize intellectual structures, identify thematic clusters, and trace the conceptual evolution of research domains (29–31). Such approaches can delineate mature versus emerging topics, highlight central contributors, and uncover neglected but high-impact areas of inquiry.

Accordingly, this bibliometric and science mapping study aims to systematically map the global knowledge structure, thematic evolution, and research fronts of kaempferol-related antidiabetic studies. By quantitatively organizing the expanding literature, this analysis seeks to identify mature and emerging research themes and provide a structured research roadmap to guide future investigations.

METHODS

This study employed a thematic bibliometric approach to map the intellectual structure, thematic distribution, and emerging research fronts related to kaempferol as an antidiabetic agent. Data were retrieved from the Scopus database using the search query: "kaempferol AND (antidiabetic OR diabetes OR hyperglycemia OR 'insulin resistance')", covering the period 2000–2025. The search was conducted on 23 October 2025, limited to English-language journal articles. Non-article document types (e.g., reviews, conference papers, book chapters, and editorials) were excluded to ensure analytical consistency. All bibliographic metadata were exported in CSV format. Prior to analysis, the dataset was examined to identify and remove duplicate records using spreadsheet software. No manual screening of titles or abstracts was performed; document selection was entirely based on the predefined search strategy and Scopus filtering criteria to ensure objectivity and reproducibility. The cleaned dataset was subsequently analyzed using VOSviewer for network visualization (32) and Biblioshiny, the web interface of the Bibliometrix R-package (33).

The analysis comprised three main stages: 1) Conceptual structure analysis using co-word analysis to explore relationships among author keywords and reveal the intellectual foundations of the field. 2) Thematic mapping, based on Callon's centrality and density metrics, which categorize clusters into motor, basic, niche, and emerging/declining themes. 3) Topic trend and thematic evolution analysis, applying VOS clustering algorithms to trace the temporal development and transformation of research themes (29–31).

This analytical workflow follows the science mapping framework emphasizing the longitudinal and multidimensional understanding of scientific knowledge dynamics. By integrating both quantitative and visual analyses, this approach provides a comprehensive view of how kaempferol-related research has evolved and where future studies particularly those incorporating omics-based studies approaches are likely to advance.

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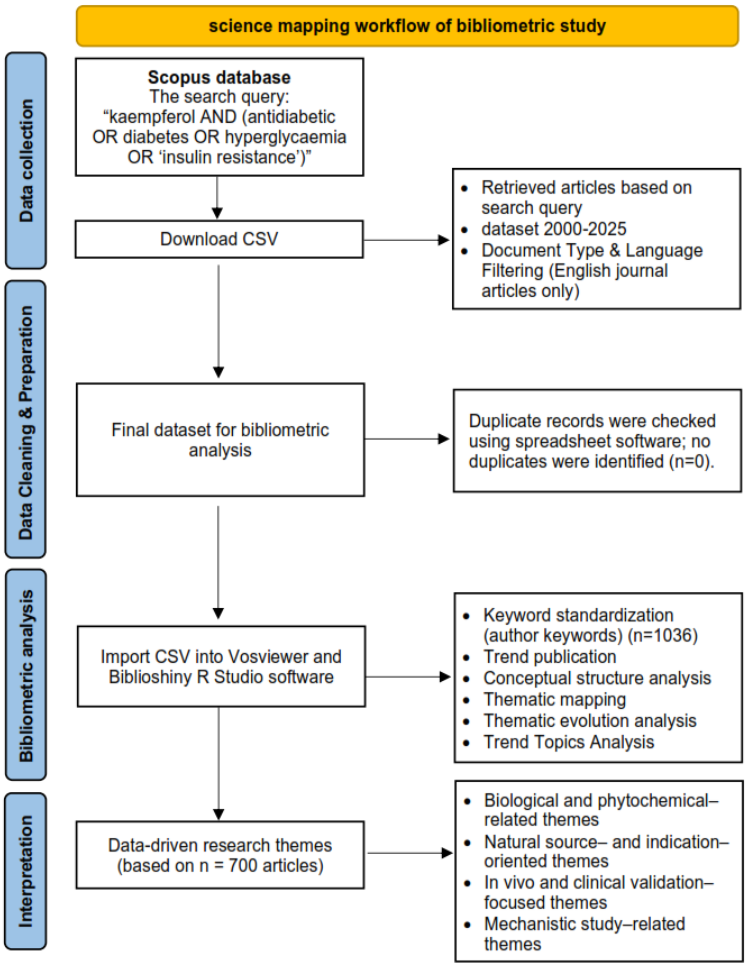

Figure 1. Science mapping workflow of bibliometric study

Figure 1 illustrates the science mapping workflow of the bibliometric study, including data retrieval, preprocessing, and analytical stages.

RESULTS

Results this bibliometric analysis aimed to map the intellectual landscape and research evolution of kaempferol as an antidiabetic agent from 2000 to 2025. Using VOSviewer and Biblioshiny (R Studio), conceptual, thematic, and trend maps were generated to examine the structural and developmental patterns of the field. A total of 700 scientific documents were retrieved from the Scopus database, published across 265 journal sources. The publication trend revealed an annual growth rate of 19.5%, reflecting a steadily increasing research interest over the past two decades. A total of 4,089 authors contributed to the corpus, with an average of 6.32 co-authors per paper, indicating a strong collaborative culture. Approximately 29.29% of the studies involved international collaboration, suggesting that research on kaempferol has evolved into a globally interconnected and multidisciplinary topic. The average citation rate of 22.56 per document highlights the scientific influence and relevance of this research domain within phytochemistry and metabolic pharmacology. These metrics confirm the significant and accelerating development of kaempferol-related research as an antidiabetic agent. These descriptive patterns provide a foundation for the subsequent thematic and conceptual analyses, offering deeper insight into how the field has evolved and where it is heading.

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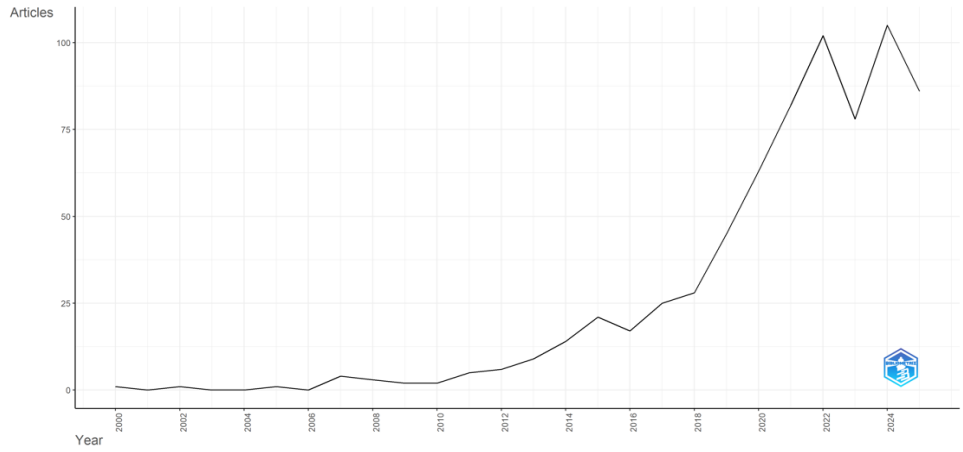

Figure 2. Trend publication since 2000 – 2025

Figure 2 reveals a remarkable surge in scholarly interest concerning kaempferol-related research from 2000 to 2025. For nearly a decade (2000–2010), the number of publications remained minimal, indicating that kaempferol was still a relatively underexplored compound within the scientific community. However, a steady growth became evident after 2012, followed by an exponential increase beginning around 2018, culminating in publication peaks in 2022 and 2024.

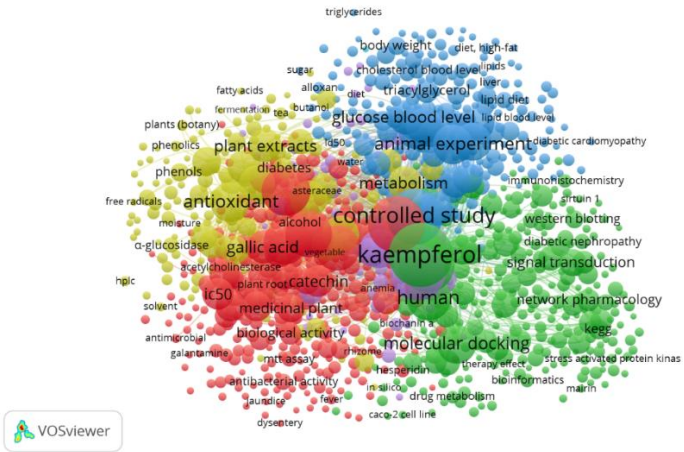

Figure 3. Keyword Co-occurrence Network Map

Figure 3, The keyword co-occurrence analysis revealed four thematic clusters that shape the intellectual landscape of kaempferol-related antidiabetic research. These clusters represent data-driven research themes emerging from bibliometric mapping.

The first cluster corresponds to biological and phytochemical–related themes (red cluster), emphasizing biological activity assessment, IC_{50} values, and phytochemical constituents such as gallic acid derived from plant roots. The second cluster reflects natural source– and indication–oriented themes (yellow cluster), focusing on plant extracts, phenolic compounds, and their association with diabetes-related conditions. The third cluster represents in vivo and clinical validation–focused themes (blue cluster), encompassing animal experiments, controlled studies, and glycemic outcome measures such as blood glucose levels. The fourth cluster captures mechanistic investigation–related themes (green cluster), highlighting computational and systems-based approaches, including molecular docking and network pharmacology.

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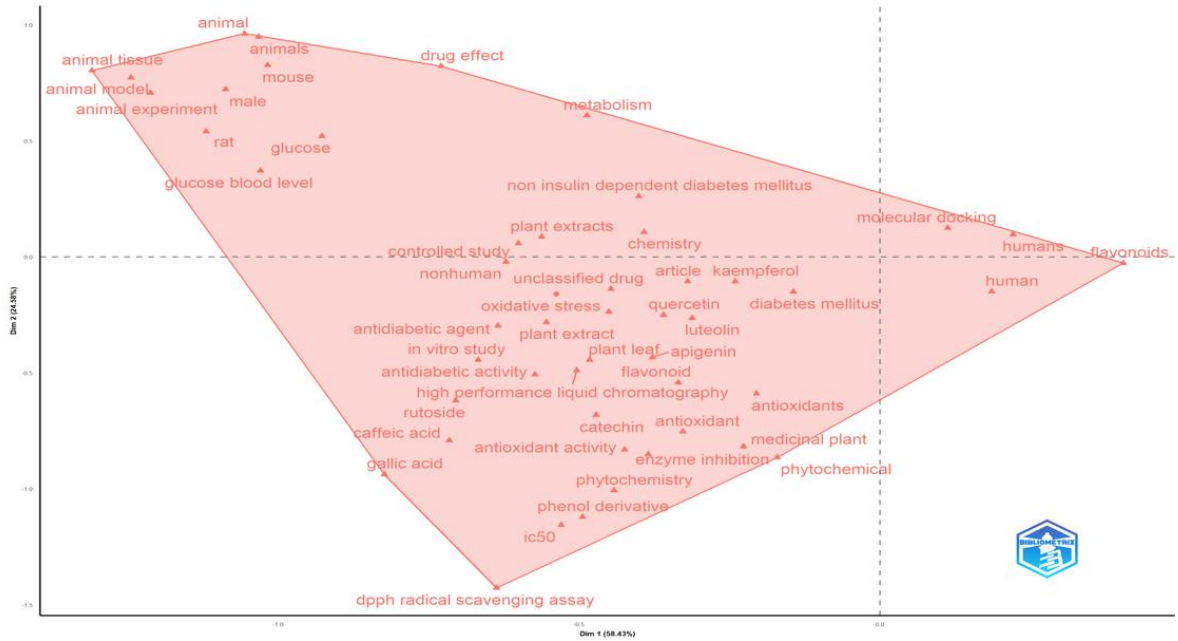

Figure 4. Conceptual Structure Map

Figure 4 presents a conceptual structure map of kaempferol as antidiabetic research generated using Multiple Correspondence Analysis (MCA). In this map, each red point represents an author keyword, and their spatial distribution reflects thematic proximity, whereby keywords located closer to each other tend to co-occur within the same body of literature.

The MCA plot displays the distribution of keywords across two principal dimensions. Dimension 1 (59.43%), represented on the horizontal axis, suggests a gradient ranging from analytical and phytochemical–oriented research on the left to molecular and mechanistic–oriented studies on the right. Dimension 2 (11.62%), represented on the vertical axis, differentiates in vivo experimental studies in the upper region from in vitro and computational approaches in the lower region. Together, these dimensions reflect dominant thematic association patterns that have emerged in kaempferol-related research over the past two decades.

Keywords located on the left side of the horizontal axis, such as DPPH radical scavenging assay, gallic acid, plant extract, and phytochemical, are primarily associated with experimental assays and chemical characterization. This clustering reflects a strong emphasis on compound identification and bioactivity screening, which frequently characterizes early or foundational investigations in natural product research.

In contrast, the right side of the map is characterized by keywords such as molecular docking, flavonoids, human, and diabetes mellitus, indicating a growing orientation toward mechanistic and biomedical investigations. This thematic grouping reflects the increasing integration of computational modeling and biological approaches aimed at elucidating the interactions of kaempferol with enzymes, receptors, and metabolic pathways relevant to chronic metabolic disorders.

Additionally, the upper-left quadrant includes keywords such as animals, oxidative stress, glucose, and fasting blood glucose level, which are commonly associated with in vivo metabolic studies, particularly in experimental models of diabetes and oxidative stress. The spatial positioning of these terms suggests a thematic linkage between preclinical animal experimentation and biochemical assessments, highlighting a translational research focus connecting phytochemical characterization with disease-oriented validation.

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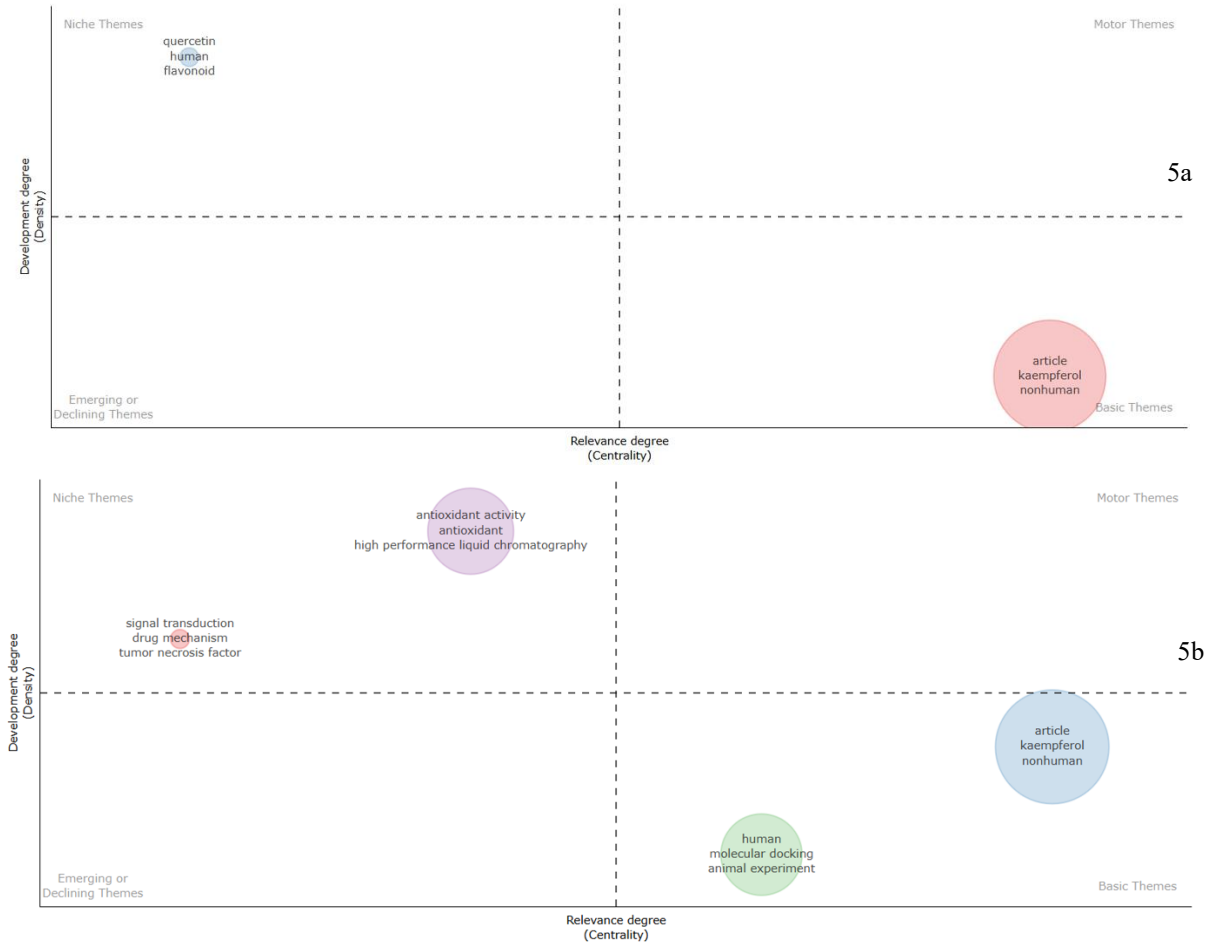

Figure 5a-5b – Thematic Evolution Analysis by Biblioshiny R Studio

Figures 5a–5b present the thematic evolution analysis, also referred to as the thematic map or strategic diagram, which positions research themes according to two dimensions: the X-axis (Centrality), representing the relevance of a theme within the overall research field, and the Y-axis (Density), indicating the degree of internal development or cohesion of each theme.

The thematic evolution analysis illustrates changes in research emphasis on kaempferol-related studies over the past two decades. During the early period (2000–2015), themes associated with kaempferol are predominantly located within the basic themes quadrant, characterized by keywords such as article, kaempferol, and nonhuman. The positioning of these keywords suggests that kaempferol-related research functions as a highly relevant but relatively less internally developed thematic area during this phase. In contrast, keywords such as quercetin, human, and flavonoid are positioned within the niche themes quadrant, indicating topics with higher internal cohesion but more limited connectivity to the broader research structure.

In the subsequent period (2016–2025), a discernible thematic shift is observed, reflecting increasing diversification of research topics. While kaempferol and nonhuman remain within the basic themes quadrant, additional clusters such as molecular docking and animal experiment emerge, indicating an expanding focus on mechanistic exploration and preclinical investigation. Furthermore, keywords including antioxidant activity, antioxidant, and high-performance liquid chromatography appear within the niche themes quadrant, highlighting the growing prominence of analytical and bioactivity-oriented methodologies. Meanwhile, terms such as signal transduction, drug mechanism, and tumor necrosis factor are positioned within the emerging or declining themes quadrant, suggesting thematic areas undergoing structural transition within the research landscape.

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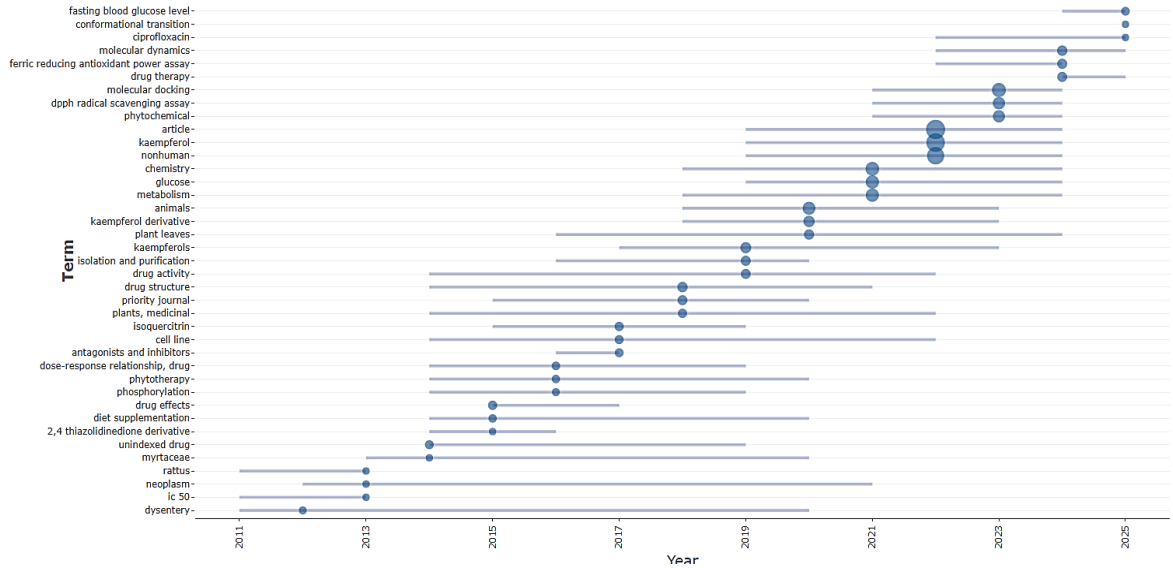

Figure 6 – Trend Topics Analysis (2000–2025) by Biblioshiny R Studio

Figure 6 presents the trend topic analysis of kaempferol-related research from 2000 to 2025, illustrating temporal changes in the prominence of research themes based on keyword frequency over time. In the early period (prior to 2015), research topics are dominated by broad pharmacological and pathological terms such as neoplasms, dysentery, and unindexed drug, reflecting an initial exploratory phase characterized by general investigations of flavonoid-related bioactivity.

Between 2015 and 2018, a shift in thematic emphasis is observed, with the emergence of keywords such as antagonists and inhibitors, dose–response relationship, and phytotherapy. The increased occurrence of these terms indicates a growing focus on biological efficacy and therapeutic relevance within kaempferol-related studies.

From 2019 to 2022, the research landscape becomes more diversified, with frequent appearances of keywords including kaempferol derivatives, drug activity, metabolism, and glucose. This period reflects an expanding integration of biochemical, pharmacological, and metabolic perspectives, particularly in relation to diabetes-related research contexts.

In the most recent period (2023–2025), trend topics are characterized by more specialized and method-oriented keywords, such as molecular docking, DPPH radical scavenging assay, ferric reducing antioxidant power assay, and fasting blood glucose level. The prominence of these terms suggests an increased emphasis on mechanistic investigation, antioxidant evaluation, and glycemic outcome assessment within kaempferol-related research.

DISCUSSION

This discussion interprets the bibliometric findings by contextualizing publication trends, thematic structures, and methodological evolution within the broader development of kaempferol research in diabetes management. Overall, the bibliometric landscape from 2000 to 2025 reflects a clear progression from foundational phytochemical studies toward a multidisciplinary research field integrating molecular nutrition, pharmacology, and translational science.

Beyond thematic labeling, the keyword co-occurrence analysis reveals converging mechanistic emphases in kaempferol-related antidiabetic research. Dominant and emerging keywords associated with molecular docking, AMPK signaling, α-glucosidase inhibition, oxidative stress, and inflammatory modulation indicate a shift toward multi-target metabolic regulation rather than single-pathway intervention. These bibliometric patterns are consistent with previous reviews reporting that kaempferol improves insulin sensitivity through AMPK activation, suppresses postprandial hyperglycemia via α-glucosidase inhibition, and attenuates oxidative stress and low-grade inflammation implicated in insulin resistance (34–36). The recent appearance of gene expression- and metabolomics-related terms further suggests an increasing interest in systems-level mechanisms, positioning kaempferol within contemporary

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nutrigenomic and precision nutrition frameworks (16,20,37).

The conceptual evolution of the field is further illustrated by the Multiple Correspondence Analysis. Classical research approaches, characterized by antioxidant assays and crude extract evaluations, are thematically separated from contemporary mechanistic and computational studies. This transition reflects not only methodological advancement but also a conceptual shift—from effect-oriented screening to mechanism-driven inquiry. Similar transitions have been noted in recent reviews of flavonoid research, where antioxidant capacity is no longer considered sufficient evidence of therapeutic relevance without molecular validation (38,39).

Despite these advances, the bibliometric evidence indicates a persistent translational gap. The predominance of in vitro and animal-based keywords, coupled with limited representation of human clinical terms, suggests that kaempferol research remains largely preclinical. This observation aligns with broader nutraceutical development literature, which highlights challenges in translating flavonoid efficacy from experimental models to clinical settings due to pharmacokinetic limitations, regulatory barriers, and insufficient large-scale trials (40). Consequently, kaempferol appears to occupy an early-to-intermediate position within the nutraceutical and drug development pipeline.

Importantly, the bibliometric maps reveal that keywords related to bioavailability enhancement and drug delivery systems, such as nanoparticles, nanoemulsions, liposomes, or formulation strategies, are largely absent from the main thematic clusters. This absence highlights a critical research gap. Numerous pharmaceutical reviews have emphasized that kaempferol and structurally related flavonoids exhibit poor aqueous solubility, extensive first-pass metabolism, and limited systemic exposure, all of which constrain their clinical applicability (21,41–43). The limited bibliometric visibility of formulation-based research suggests that delivery strategies have not yet become a central focus, despite their recognized importance in bridging mechanistic efficacy with therapeutic translation. This gap coincides with ongoing advances in omics technologies and computational modeling, which offer powerful tools to elucidate the molecular basis of kaempferol's biological activities in future studies (20,44–49).

Although this study did not quantitatively analyze geographic publication patterns, the thematic prominence of phytotherapy-related research suggests substantial contributions from regions where kaempferol-rich plants are traditionally used, particularly in Asia. Traditional medical systems such as Traditional Chinese Medicine and Ayurveda have long employed flavonoid-containing plants for metabolic disorders, which likely influenced early research trajectories and continue to shape contemporary scientific inquiry (20,50). This cultural–biological context contributes to the global knowledge structure of kaempferol research and underscores the role of ethnopharmacology as a driver of modern nutraceutical science (20).

From a safety perspective, bibliometric mapping revealed minimal emphasis on toxicity, safety, or long-term adverse effects. This finding mirrors observations from recent flavonoid safety reviews, which note that kaempferol is generally regarded as safe at dietary levels. Preclinical safety evidence further supports this bibliometric observation. In in vivo screening studies, kaempferol has not been reported to exhibit carcinogenic or overt toxic effects. For instance, long-term oral administration of kaempferol at a concentration of 0.04% for up to 540 days in rats did not result in carcinogenic outcomes. Similarly, administration of kaempferol at doses as high as 2,000 mg/kg body weight showed no observable signs of acute toxicity, with no evidence of nephrotoxicity or hepatotoxicity reported. In addition to its metabolic effects, kaempferol has been described to exert chemopreventive, chemoprotective, and restorative conditioning effects in a treatment-dependent manner. Moreover, nanoformulated kaempferol has demonstrated cytotoxic activity against colon cancer cells and has been explored as a potential anticancer drug delivery system. Importantly, available preclinical evidence suggests that kaempferol is less toxic to normal human cells while exhibiting comparatively higher cytotoxicity toward cancer cells. However, despite these encouraging findings, systematic long-term safety evaluations and well-designed human studies remain limited, underscoring the need for further toxicological and clinical investigations before translational application (14,51).

Taken together, these findings portray kaempferol research as an evolving scientific narrative—progressing from basic phytochemical characterization to mechanistic and systems-level investigation.

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Future research should prioritize integrative multi-omics approaches, formulation and delivery strategies, and rigorously designed clinical studies to advance kaempferol toward evidence-based application in diabetes management.

Synthesis of Findings

Collectively, the analyses from the co-occurrence network, multiple correspondence analysis (MCA), and thematic mapping delineate a cohesive intellectual structure within this research domain. Central keywords such as oxidative stress, insulin resistance, and inflammation remain the conceptual backbone, while peripheral but expanding themes bioavailability, and gene modulation suggest a diversification of methodological approaches. The thematic evolution highlights a gradual shift from descriptive antioxidant studies toward integrative analyses linking molecular signaling with clinical biomarkers. Furthermore, the trend topic analysis reveals that contemporary research increasingly emphasizes molecular docking, metabolomics, and nutrigenomic profiling, indicating a methodological advancement toward data-driven, system-level investigations. Despite this progress, certain knowledge gaps persist, particularly concerning in vivo biotransformation, pharmacokinetic profiling, and the clinical translation of kaempferol-derived metabolites in diabetic contexts.

These integrative bibliometric insights explicitly validate the primary objective of this investigation to identify and substantiate the research gap concerning the integration of omics-based approaches within kaempferol research. The observed clustering patterns and thematic progressions affirm that while molecular and pharmacological mechanisms have been extensively explored, studies incorporating metabolomics and nutrigenomics remain underrepresented. This imbalance underscores a critical need for multidimensional frameworks that connect bioavailability, gene modulation, and systemic metabolic outcomes. Consequently, the findings provide a clear research roadmap encouraging a paradigm shift from isolated mechanistic exploration to holistic, data driven investigations laying the groundwork for developing kaempferol as a personalized nutraceutical and integrative therapeutic agent for diabetes management.

Scientific Implications

The scientometric evidence underscores an important paradigm shift in kaempferol research from reductionist antioxidant (phytochemistry) characterization to systems-level nutrigenomic investigation. This intellectual evolution not only refines the understanding of kaempferol's mechanistic pathways but also broadens its translational prospects for nutraceutical innovation. Future research should prioritize integrative approaches that connect nutrigenomic and metabolomic data with functional outcomes in diabetic models. Moreover, cross-disciplinary collaboration between pharmacologists, nutrition scientists, and molecular biologists will be essential to bridge experimental findings with personalized nutrition frameworks. By mapping the field's conceptual and methodological trajectory, this synthesis provides a foundation for precision-based nutraceutical development, aligning kaempferol research with contemporary paradigms in molecular nutrition and metabolic health.

CONCLUSION

The scientometric evaluation delineates a clear developmental trajectory in kaempferol research within the context of diabetes management. Over the past two decades, the field has evolved from descriptive antioxidant and anti-inflammatory studies (phytochemistry) toward a multidisciplinary framework integrating molecular pharmacology, nutrigenomics, and metabolomics. This intellectual transition reflects a growing recognition of kaempferol as a bioactive compound with both preventive and therapeutic potential. Despite these advancements, notable gaps persist particularly in the integration of omics-based analyses, in vivo biotransformation studies, pharmacokinetic modeling, and the clinical translation of kaempferol derived metabolites.

Future research should therefore emphasize systems-level approaches that connect nutrigenomics, and metabolomics data with physiological outcomes in diabetic models. Strengthening cross-disciplinary collaborations among pharmacologists, molecular biologists, and nutrition scientists

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will be essential to bridge mechanistic findings with personalized nutrition frameworks. Through this integrative lens, kaempferol research may progress toward its full potential as a precision-based nutraceutical for diabetes prevention and management.

DECLARATION OF THE USE OF AI

The authors declare that no artificial intelligence (AI), AI-assisted technologies, or large language models (LLMs) were used in the conception of the study, data analysis, or the drafting, writing, and editing of this manuscript. The only exception is the graphical abstract, which was created using the design platform Illustrae (https://illustrae.co/). The authors take full responsibility for the content and accuracy of the graphical abstract and the entire manuscript.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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