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Scientific production on enzymatic hydrolysis of bovine whey and its bioactive peptides: A bibliometric approach

Produção científica sobre hidrólise enzimática do soro de leite bovino e seus peptídeos bioativos: Uma abordagem bibliométrica

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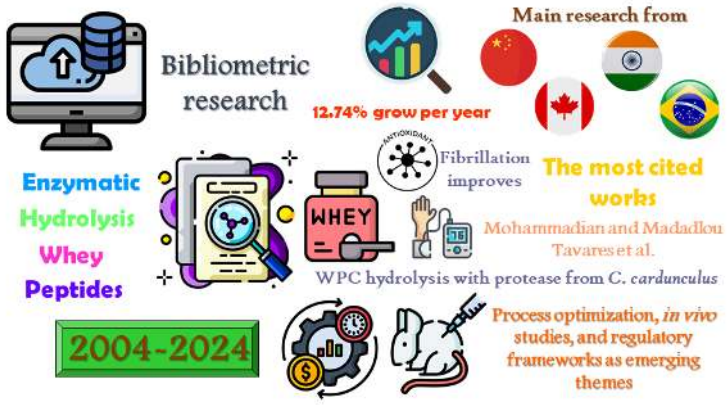
Abstract
The increasing interest in the health benefits of whey-derived bioactive peptides highlighted the need for a comprehensive understanding of their production and applications. This study analyzed the global research landscape on the enzymatic hydrolysis of bovine whey and its bioactive peptides from 2004 to 2024. A bibliometric approach was used to identify key themes, trends, and collaborative efforts. Data were collected from 183 documents across 80 sources, and thematic and Multiple Correspondence Analysis (MCA) maps were employed to categorize research themes and reveal central clusters. The analysis demonstrated a 12.74% annual growth in publications, with significant contributions from countries such as China, Canada, India, and Brazil. Key journals like "LWT-Food Science and Technology" and "Food Chemistry" were identified as leading sources. The functional properties of whey-derived peptides, including antioxidant, antihypertensive, antidiabetic, antithrombotic, and hypocholesterolemic effects, were highlighted, underscoring their potential applications in the food and pharmaceutical industries. The collaborative nature of the research was evident, with an average of 4.92 co-authors per paper and international collaborations accounting for 26.78% of the documents. The findings emphasized the therapeutic potential of bioactive peptides and the need for continued exploration of novel technologies and applications. It was concluded that the enzymatic hydrolysis of whey proteins remains dynamic and interdisciplinary, with promising avenues for future research and development in enhancing health outcomes and innovative food solutions.

Keywords: Enzymatic hydrolysis. Bioactive peptides production. Whey protein utilization. Functional food applications. Food and pharmaceutical applications.

Resumo
O crescente interesse nos benefícios à saúde dos peptídeos bioativos derivados do soro de leite destacou a necessidade de uma compreensão abrangente de sua produção e aplicações. Este estudo analisou o cenário global de pesquisa sobre a hidrólise enzimática do soro de leite bovino e seus peptídeos bioativos de 2004 a 2024. Uma abordagem bibliométrica foi usada para identificar os principais temas, tendências e esforços colaborativos. Os dados foram coletados de 183 documentos em 80 fontes, e mapas temáticos e de Análise de Correspondência Múltipla (MCA) foram empregados para categorizar temas de pesquisa e revelar clusters centrais. A análise demonstrou um crescimento anual de 12.74% nas publicações, com contribuições significativas de países como China, Canadá, Índia e Brasil. Periódicos importantes como "LWT-Food Science and Technology" e "Food Chemistry" foram identificados como fontes líderes. As propriedades funcionais dos peptídeos derivados do soro de leite, incluindo efeitos antioxidantes, anti-hipertensivos, antidiabéticos, antitrombóticos e hipocolesterolêmicos, foram destacadas, ressaltando suas potenciais aplicações nas indústrias alimentícia e farmacêutica. A natureza colaborativa da pesquisa foi evidente, com uma média de 4.92 coautores por artigo e colaborações internacionais respondendo por 26.78% dos documentos. As descobertas enfatizaram o potencial terapêutico dos peptídeos bioativos e a necessidade de exploração contínua de novas tecnologias e aplicações. Concluiu-se que a hidrólise enzimática das proteínas do soro de leite permanece dinâmica e interdisciplinar, com caminhos promissores para futuras pesquisas e desenvolvimento na melhoria dos resultados de saúde e soluções alimentares inovadoras.

Palavras-chave: Hidrólise enzimática. Produção de peptídeos bioativos. Utilização de proteína de soro de leite. Aplicações de alimentos funcionais. Aplicações alimentícias e farmacêuticas.

Graphical Abstract



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ROYALDATASET

1. Introduction

Bovine whey, a by-product of the dairy industry, has gained increasing significance due to its high production volume and diverse potential applications. In cheese production, about 1 kg of whey is derived from every 10 liters of milk (Solís Oba et al., 2023). This by-product accounts for 80% to 90% of processed milk's volume and contains roughly 50% of its nutrients, including soluble proteins, lactose, and minerals, making it a valuable resource (Guedes et al., 2023; Salazar-Manzanares et al., 2023). Rich in *α*-lactalbumin, *β*-lactoglobulin, lactoferrin, lactose, and lipids, bovine whey offers high nutritional value and functional properties, widely used in food production for its emulsifying, stabilizing, and flavor-enhancing capabilities (Aponte Colmenares et al., 2023; Muñoz et al., 2019; Rivera-Rojas et al., 2024).

The generation of antihypertensive, antioxidant, and immunomodulatory peptides from bovine whey digestion or hydrolysis is an emerging research area, making them promising candidates for nutraceuticals and functional foods (Barrero et al., 2021; Garcia-Castro et al., 2022). Valorizing bovine whey reduces environmental pollution and opens new opportunities in the food and pharmaceutical industries (Motta-Correa & Mosquera M., 2022; Tolentino-Barroso et al., 2023; Williams Zambrano & Dueñas Rivadeneira, 2021).

Enzymatic hydrolysis is a bioprocess in which enzymes transform high molecular weight proteins into smaller fragments with biological activity that benefit health. (Eberhardt et al., 2021; Islas-Martínez et al., 2023; Mora & Toldrá, 2023; Pérez-Escalante et al., 2022; Samtiya et al., 2022). That process favors conventional methods like chemical hydrolysis because it enhances protein bioactivity, producing peptides with superior biological functions (Murtaza et al., 2022; Salami et al., 2010). This process is more specific, allowing precise control over peptide size and composition, and is gentler, better preserving the functional and bioactive properties of the peptides while minimizing undesirable by-products (Aponte Colmenares et al., 2023; Muñoz et al., 2019). Additionally, enzymatic hydrolysis is more sustainable and environmentally friendly, utilizing milder reaction conditions and moderate temperatures (Román & Linares, 2011).

The types of enzymes commonly employed in the enzymatic hydrolysis of bovine whey include proteases derived from microbial, plant, and animal sources. Microbial proteases, such as those from *Bacillus* and *Aspergillus* species, are particularly favored due to their broad specificity and efficiency in hydrolyzing whey proteins (Eberhardt et al., 2021; Mora & Toldrá, 2023; Rivera-Rojas et al., 2024; Salazar-Manzanares et al., 2023). Additionally, plant-derived enzymes like bromelain and papain have been utilized for their ability to produce specific peptide sequences that can exhibit targeted biological activities (Murtaza et al., 2022). The choice of enzyme can significantly influence the yield and bioactivity of the resulting peptides, underscoring the importance of selecting appropriate enzymatic conditions for optimal hydrolysis (Eberhardt et al., 2021; Mora & Toldrá, 2023; Samtiya et al., 2022).

Diverse bioactive peptides from food sources contribute to chronic disease prevention. Antioxidant peptides reduce oxidative stress by scavenging free radicals linked to cardiovascular diseases and cancer (Costa et al., 2023; Duffuler et al., 2022; Han et al., 2021). Antihypertensive peptides, by inhibiting angiotensin-converting enzyme (ACE), help regulate blood pressure (Manzanares et al., 2019; Ryan et al., 2011). Peptides with antidiabetic properties inhibit dipeptidyl peptidase IV (DPP-IV), impacting glucose metabolism (Iwaniak et al., 2018; Yan et al., 2019). Additionally, antithrombotic peptides can prevent platelet aggregation, reducing thrombosis risk (Cheng et al., 2024; Yu et al., 2011).

The effectiveness of these peptides depends on their bioavailability, which is influenced by their stability during digestion and their absorption in the intestines (Dave et al., 2014; Ryan et al., 2011). Structural features like hydrophobicity and length impact their biological activity, with peptides rich in hydrophobic amino acids often showing more potent effects (Acquah et al., 2018; Devita et al., 2021). Therefore, a comprehensive understanding of these relationships is necessary to develop effective nutraceuticals for chronic disease prevention, which can, in turn, contribute to improving public health (Costa et al., 2023; Duffuler et al., 2022; Iwaniak et al., 2018; Mendoza-Jiménez et al., 2018).

Bioactive peptides enhance product functionality and health benefits across the food, pharmaceutical, and nutraceutical industries. Bovine whey-derived peptides, known for their diverse properties, are being optimized through enzymatic and fermentation processes, including lactic acid bacteria, to boost their bioactivity and expand their use in functional foods (Eberhardt et al., 2021; Helal et al., 2023; Piccolomini et al., 2015; Tagliazucchi et al., 2019).

A bibliometric study on bovine whey-derived bioactive peptides is necessary to understand the current research landscape and emerging trends. Such an analysis can guide future studies and industrial applications, fostering innovation in functional foods and nutraceuticals while promoting sustainability and valorization of dairy by-products. Mapping existing knowledge will also help identify research gaps, enabling a more strategic approach to enhancing human health and sustainability in the food industry (Costa et al., 2023; Herrera-Ponce et al., 2019; Rodriguez, 2020).

In line with the above, this contribution aimed to analyze the scientific production of the enzymatic hydrolysis of bovine whey and its bioactive peptides with functional properties (antioxidant, antihypertensive, antidiabetic, antithrombotic, hypocholesterolemic) using the Web of Science® (WoS) database, to identify the main research trends, prominent thematic areas, and international collaborations in this field.

2. Methodology

The present study used a bibliometric approach to analyze the scientific production of the enzymatic hydrolysis of bovine whey and bioactive peptides with beneficial properties on non-communicable diseases. Data was collected in the Web of Science® (WoS) database, using the advanced search mode, following the procedure described in previous studies (García-Curiel et al., 2024; Pérez-Flores et al., 2024). The search was conducted on August 26, 2024, using the following logical search query: 'TS=("enzymatic hydrolysis" AND ("bovine whey" OR whey) AND peptides AND (antioxidant* OR antihypertensive OR antidiabetic OR antithrombotic OR hypocholesterolemic OR "bioactive peptides"))'. The search scope was restricted to experimental scientific English articles published between 2004 and 2024.

The search results were downloaded as a single BibTeX file (savedrecs.bib) to streamline handling and analysis. The records contained essential information, including authors, titles, abstracts, keywords, affiliations, citations, and other relevant metadata. The bibliometric analysis was conducted using R version 4.1.2 (2021-11-01) "Bird Hippie" and the 'bibliometrix' package version 4.1.4 and its graphical interface, 'biblioshiny'. Finally, the results were interpreted based on the evolution of

research on bovine whey bioactive peptides, emphasizing their functional properties. This provided a comprehensive overview of current trends and key research areas.

3. Results and Discussion

3.1. Scientific production from 2004 to 2024 timespan

The logical search function was designed to identify articles in WoS that focused on the enzymatic hydrolysis of bovine whey, explicitly targeting the resulting peptides and their bioactive properties. The search targeted studies that mentioned terms such as “enzymatic hydrolysis” in combination with “bovine whey” or simply “whey”, along with “peptides”. Articles discussing specific properties of these peptides, such as their antioxidant, antihypertensive, antidiabetic, antithrombotic, and hypocholesterolemic capabilities, or those explicitly referring to "bioactive peptides" were included. The asterisk (*) in “antioxidant*” allowed for the retrieval of all variations of the term, such as “antioxidant” or “antioxidants”.

A descriptive summary of the scientific production of the enzymatic hydrolysis of bovine whey and its bioactive peptides with functional properties from 2004 to 2024 was provided in **Table 1**. Over these 20 years, 183 documents were published across 80 different sources, including scientific journals and other academic media. The research area experienced a sustained annual growth rate of 12.74%, indicating a steady increase in interest, likely driven by the growing recognition of whey-derived peptides’ functional properties and their potential applications in the food and pharmaceutical industries. This expansion reflected a field marked by constant innovation and diversification of applications.

The average number of citations per document, 23.6, suggested a significant impact on the scientific community, with the works widely referenced in subsequent studies. The relatively recent nature of literature, with an average document age of 5.66 years, reinforced the timeliness and dynamism of the research area. Additionally, many author keywords (610) and Keywords Plus (556) were observed, highlighting the thematic diversity and richness of approaches within the field.

The analysis of author collaboration revealed that no single-authored documents were present, emphasizing the collaborative nature of research in this area. The average number of co-authors per document was 4.92, reflecting the teamwork and interdisciplinary efforts required to address the challenges in researching bioactive peptides. Furthermore, 26.78% of the papers involved international collaborations, underscoring the global relevance of the topic and the cooperation between researchers from different countries to advance this field.

Table 1 Descriptive summary of scientific production on enzymatic hydrolysis of bovine whey and its bioactive peptides (2004-2024).

Description	Results
MAIN INFORMATION ABOUT DATA	
Timespan	2004-2024
Sources (Journals, Books, etc)	80
Documents	183
Annual Growth Rate %	12.74
Document Average Age	5.66
Average citations per doc	23.6
DOCUMENT CONTENTS	
Keywords Plus (ID)	556
Author’s Keywords (DE)	610
AUTHORS	
Authors	768
Authors of single-authored docs	0
AUTHORS COLLABORATION	
Single-authored docs	0
Co-Authors per Doc	4.92
International co-authorships %	26.78
DOCUMENT TYPES	
Article	183

Fig. 1 shows an overview of scientific production from 2004 to 2024 timespan. **Fig. 1a** shows a bar chart depicting the number of articles published per year from 2004 to 2013, showing a clear trend of increasing research output over time, with some fluctuations. From 2004 to 2006, in the early years, they exhibited minimal activity, with only one article published each year. This steady but low output continued until 2007 when a slight increase to two articles was observed. Notably, there is a gap in 2008, where no articles were published, potentially indicating a temporary decline in research activity or other external factors affecting publication.

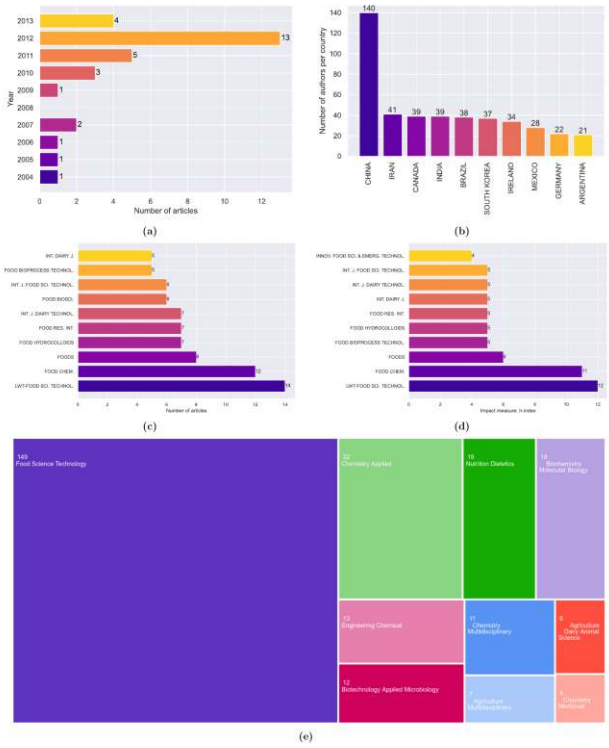

Fig. 1 Overview of scientific production on enzymatic hydrolysis of bovine whey and its bioactive peptides from 2004 to 2024 timespan. (a) Annual publication count over time, (b) Number of authors per country, (c) Top journals by number of articles published, (d) h-index of leading journals, and (e) Treemap chart of research article distribution across Web of Science® categories.

The following years demonstrate a significant rise in output, particularly from 2010 onwards, where the number of articles jumps from three in 2010 to a peak of thirteen in 2012. This sharp increase suggests a growing interest and investment in the research area. The slight dip to four articles in 2013 could indicate a normalization of output after the peak or possibly a shift in research focus. The chart reflects a trajectory of increasing academic engagement, with a notable acceleration in the early 2010s, highlighting heightened research activity.

Fig. 1b shows a bar chart illustrating the distribution of authors across different nations, highlighting China’s dominance with 140 authors, significantly surpassing other countries. Iran, Canada, India, and Brazil also contribute a substantial number of authors, ranging between 38 and 41. South Korea and Ireland follow closely with 37 and 34 authors, respectively. Mexico, Germany, and Argentina are represented with fewer authors, indicating fewer but notable contributions to the research landscape. This distribution suggests a strong presence of research activities in Asia, with China leading, and also emphasizes the diverse contributions from countries across different continents. The data points to a concentration of authorship in a few key countries, reflecting potential differences in

research capacity, academic resources, and international collaboration networks.

Fig. 1c presents a bar chart showing the distribution of articles across different academic journals, emphasizing the prominence of specific sources in the field. “LWT-Food Science and Technology” leads with 14 articles, indicating its significant role as a critical platform for publishing research in this domain. “Food Chemistry” closely follows with 12 articles, underscoring its broad appeal and relevance in food science research. Other journals, such as “Foods” and “Food Hydrocolloids”, with 8 and 7 articles, respectively, also play crucial roles, particularly in niche areas related to food structure and properties.

The consistency among journals like “Food Research International”, “International Journal of Dairy Technology”, and “Food Bioscience”, each with 6 to 7 articles, reflects a well-distributed interest across various specialized fields within food science. Notably, journals focused on dairy technology, such as the “International Journal of Dairy Technology” and the “International Dairy Journal”, collectively contribute 12 articles, highlighting the importance of dairy-related research in the overall dataset. This distribution of articles across multiple journals suggests a diverse and multidisciplinary approach to food science, with each source contributing unique insights to the broader research community.

Fig. 1d presents the h-index of prominent food science and technology journals, offering insights into their impact and influence. The journal “LWT - Food Science and Technology” leads with an h-index of 12, followed closely by “Food Chemistry” with an h-index of 11, indicating their vital citation records and significant contributions to the literature. Other journals, such as “Foods and Food Bioprocess Technology”, show lower h-index values of 6 and 5, respectively, reflecting a more specialized or emerging focus in these areas. The relatively high h-index of “LWT - Food Science and Technology and Food Chemistry” suggests these journals are vital sources of highly cited research, making them crucial platforms for disseminating influential work within the discipline. This figure underscores the varying levels of impact among these journals, highlighting the importance of considering such metrics in bibliometric analyses to understand the academic reach and authority of different publication sources within the field.

Finally, **Fig. 1e** was presented as a treemap chart generated from Web of Science data, illustrating the distribution of research articles across various categories within the database. The dominant category, “Food Science Technology”, was represented by 149 records, accounting for 78.42% of the total, reflecting the primary focus of the research on food science. “Chemistry Applied” and “Nutrition Dietetics” were followed, with 32 and 19 records, respectively, making up 16.84% and 10% of the total. These categories indicated significant interdisciplinary connections between food science, applied chemistry, and nutrition. Other notable categories included “Biochemistry Molecular Biology” (9.47%) and “Engineering Chemical” (6.84%), highlighting how molecular biology techniques and chemical engineering principles were integrated into food science research. Less represented fields, such as “Biotechnology Applied Microbiology” and “Chemistry Multidisciplinary”, suggested that specialized contributions were made within the broader scope of the study.

The treemap chart effectively visualized the hierarchical importance of these categories, with more significant segments representing more substantial research activity. The central role of food science in the dataset was emphasized, while the relevant, albeit smaller, contributions from adjacent scientific fields were also showcased. The visual representation in the treemap chart helps to understand the research landscape, illustrating how various disciplines intersected and contributed to the overarching field of food science and technology.

In **Table 2**, the most globally cited documents in the field were analyzed using several key bibliometric indicators. The columns “Total Citations”, “TC per Year”, and “Normalized TC” were used to evaluate each paper’s impact and relevance. The “Total Citations” column measured each publication’s overall influence by tallying its citation count. The highest citation count was attributed to Mohammadian and Madadlou (2016) in Food Hydrocolloids, with 138 citations highlighting its significant impact.

Table 2 Most globally cited articles on enzymatic hydrolysis of bovine whey or other emerging sources and its bioactive peptides from 2004 to 2024 timespan.

Title	Journal	Total Citations (TC)	TC per Year	Normalized TC	Reference
Novel whey-derived peptides with inhibitory effect against angiotensin-converting enzyme: *In vitro* effect and stability to gastrointestinal enzymes	Peptides	124	8.86	2.38	Tavares et al. (2011)
Improvement of the antimicrobial and antioxidant activities of camel and bovine whey proteins by limited proteolysis	Journal of Agricultural and Food Chemistry	118	7.87	1.26	Salami et al. (2010)
Immunomodulating effects of whey proteins and their enzymatic digests	International Dairy Journal	108	5.14	1	Mercier et al. (2004)
Effect of heat and enzymatic treatment on the antihypertensive activity of whey protein hydrolysates	International Dairy Journal	102	5.67	1.36	Costa et al. (2007)
Adding value to the chia (*Salvia hispanica* L.) expeller: production of bioactive peptides with antioxidant properties by enzymatic hydrolysis with papain	Food Chemistry	99	16.5	3.77	Cotabarren et al. (2019)
Physicochemical and antioxidative characteristics of black bean protein hydrolysates obtained from different enzymes	Food Hydrocolloids	97	16.17	3.69	Zheng et al. (2019)
Camel milk protein hydrolysates with improved technofunctional properties and enhanced antioxidant potential in *in vitro* and in food model systems	Journal of Dairy Science	96	13.71	2.46	Al-Shamsi et al. (2018)
Functionality and antioxidant properties of tilapia (*Oreochromis niloticus*) as influenced by the degree of hydrolysis	International Journal of Molecular Sciences	95	6.33	1.01	Foh et al. (2010)
Novel angiotensin I-converting enzyme inhibitory peptides from protease hydrolysates of Qula casein: Quantitative structure-activity relationship modeling and molecular docking study	Journal of Functional Foods	85	10.63	2.13	Lin et al. (2017)

This paper addressed enhancing the antioxidant activity and functional properties of whey proteins through fibrillation, focusing on whey protein isolate (WPI) and whey protein hydrolysate (WPH). The study found that fibrillation improved antioxidant activity, foam stability, and rheological properties, with WPI forming more homogeneous fibrils. The discussions emphasized the role of enzymatic hydrolysis in enhancing these effects, noting differences between WPI and WPH in behavior and solubility, ultimately demonstrating the potential of fibrillated whey proteins in specialty foods (Mohammadian & Madadlou, 2016).

The "TC per Year" column normalized total citations by the number of years since publication, providing insight into each paper's citation velocity. Cotabarren et al. (2019) in Food Chemistry stood out with a high annual citation rate of 16.50, reflecting its rapid influence despite its recent publication. The study addressed the antioxidant activity and protein hydrolysis of chia (*Salvia hispanica* L.) expeller, aiming to optimize enzymatic hydrolysis with Papain to produce bioactive peptides. Key findings showed significant protein modifications after 30 minutes of hydrolysis, confirmed by SDS-Tricine-PAGE and MALDI-TOF/MS analyses. The discussion emphasized successfully generating low molecular weight peptides, highlighting the process's industrial application potential (Cotabarren et al., 2019). The last work is relevant because it suggests the change in antioxidant peptides from animal to vegetal sources.

The "Normalized TC" column further adjusted citation counts to account for variations in citation practices across fields and publication years. This normalization allowed for a more equitable comparison across the papers. Here, Cotabarren et al. (2019) again demonstrated a strong impact, with a normalized TC of 3.77, closely followed by Mohammadian & Madadlou (2016) with 3.53. In the same context, papers such as those by Tavares et al. (2011) in Peptides and Salami et al. (2010) in the Journal of Agricultural and Food Chemistry were highlighted for their substantial citation counts and sustained relevance over time. Meanwhile, older publications like Mercier et al. (2004) and Costa et al. (2007) in the International Dairy Journal were noted for their steady citation rates, contributing foundational knowledge to their respective fields.

The bibliometric analysis revealed that studies focused on identifying ACE-inhibitory peptides from whey protein concentrate (WPC) for potential hypertension treatments (Tavares et al., 2011) and on enhancing the antioxidant and antibacterial activities of whey proteins, particularly from camel whey (Salami et al., 2010), were highly cited due to their significant findings. Similarly, the exploration of the immunomodulating effects and complexity of whey protein products (Mercier et al. 2004), as well as the investigation of antihypertensive activity in whey protein hydrolysates under different processing conditions (Costa et al., 2007), contributed to the sustained relevance of these works, as reflected in their citation metrics.

Through their sustained citation rates and the depth of their research findings, the bibliometric analysis underscored the importance of these studies in advancing whey protein research in both foundational knowledge and applied sciences. Collectively, these works contributed to a deeper understanding of the functional properties of whey proteins and their potential applications, solidifying their status as key references in the field.

Table 2 identified vital publications that have had a lasting and significant impact on the research landscape within food science and technology and related disciplines. Using multiple citation metrics provided a comprehensive view of each paper's influence, highlighting both long-term impact and recent advancements in the field.

3.2. Authors' keywords analysis

The results of the authors' keyword analysis are presented in **Fig. 2**. **Fig. 2a** presents a word cloud generated from the terms and their respective frequencies within the dataset derived from the bibliometric analysis. The word cloud visually represents the prominence of various research topics in the literature on the enzymatic hydrolysis of bovine whey and its bioactive peptides. The most prominent terms, "enzymatic hydrolysis" (56 occurrences), "peptides" (55 occurrences), and "bioactive peptides" (49 occurrences), were highlighted, reflecting the core focus of the research field. These terms were central to the studies, emphasizing the importance of enzymatic processes in generating bioactive peptides from whey proteins and their subsequent identification and functional characterization.

"Functional properties" (47 occurrences) and "identification" (43 occurrences) were also emphasized, indicating the significant attention that had been given to the functional aspects of these peptides, particularly their antioxidant activity (29 occurrences) and the methods used for their identification and purification (26 occurrences). The inclusion of specific protein components like "beta-lactoglobulin" (33 occurrences) and "whey-protein" (30 occurrences) underscored the detailed examination of individual proteins within whey that had contributed to bioactivity. The presence of terms such as "milk", "antioxidant", "emulsifying properties", and "stability" suggested that broader interest had been placed on the physicochemical and health-related attributes of whey-derived peptides, further illustrating the diverse research avenues explored in this field.

Fig. 2b and **Fig. 2c** presented a co-occurrence network diagram and a density map, respectively, illustrating the relationships and prominence of key terms within the research on enzymatic hydrolysis of bovine whey and its bioactive peptides. **Fig. 2b** provides a network diagram. Nodes represent significant terms, and their connections indicate co-occurrences within literature. The network is divided into several clusters, each representing a group of related terms.

The central cluster, Cluster 2 ("enzymatic-hydrolysis"), shown in blue, prominently featured terms such as "enzymatic hydrolysis", "peptides", and "functional properties". These terms were the most interconnected and crucial concepts within the research field, reflecting their pivotal role in studying whey proteins and bioactive peptides. These terms' high betweenness and PageRank values underscored their central role in bridging different research topics and influencing the network. This cluster's dominance in frequency and centrality highlighted the significance of enzymatic processes and peptide functionality in the field.

Cluster 4 ("bioactive peptides"), shown in purple, included terms like "bioactive peptides", "identification", and "beta-lactoglobulin". This cluster highlighted the focus on identifying and characterizing specific bioactive components derived from whey. The high connectivity of these terms within the cluster reflected the substantial research interest in the bioactivity and functional characterization of whey-derived peptides, making this cluster crucial in understanding the bioactive potential of these compounds.

Other clusters, such as Cluster 1 ("phosphopeptides") in red, featuring terms like "pH", "impact", and "temperature", and Cluster 5 ("temperature") in orange, including terms such as "milk", "heat" and "digestion", represented more specialized areas within the broader research context. These clusters focused on the physicochemical properties and digestion-related studies of whey proteins. Despite having lower betweenness and PageRank values, indicating a more peripheral role, these clusters were

integral to the overall network, contributing to specific niche areas within the research.

Fig. 2c, the density map, visually reinforces these findings by showing areas of high term density, with the darkest regions corresponding to the most frequently occurring and interconnected terms. The terms “enzymatic hydrolysis,” “peptides,” “bioactive peptides,” and “identification” were situated in the densest area, reflecting their centrality and importance in the research landscape. This density map confirmed the central role of enzymatic processes and bioactive peptide identification in the field, aligning with the insights provided by the network analysis.

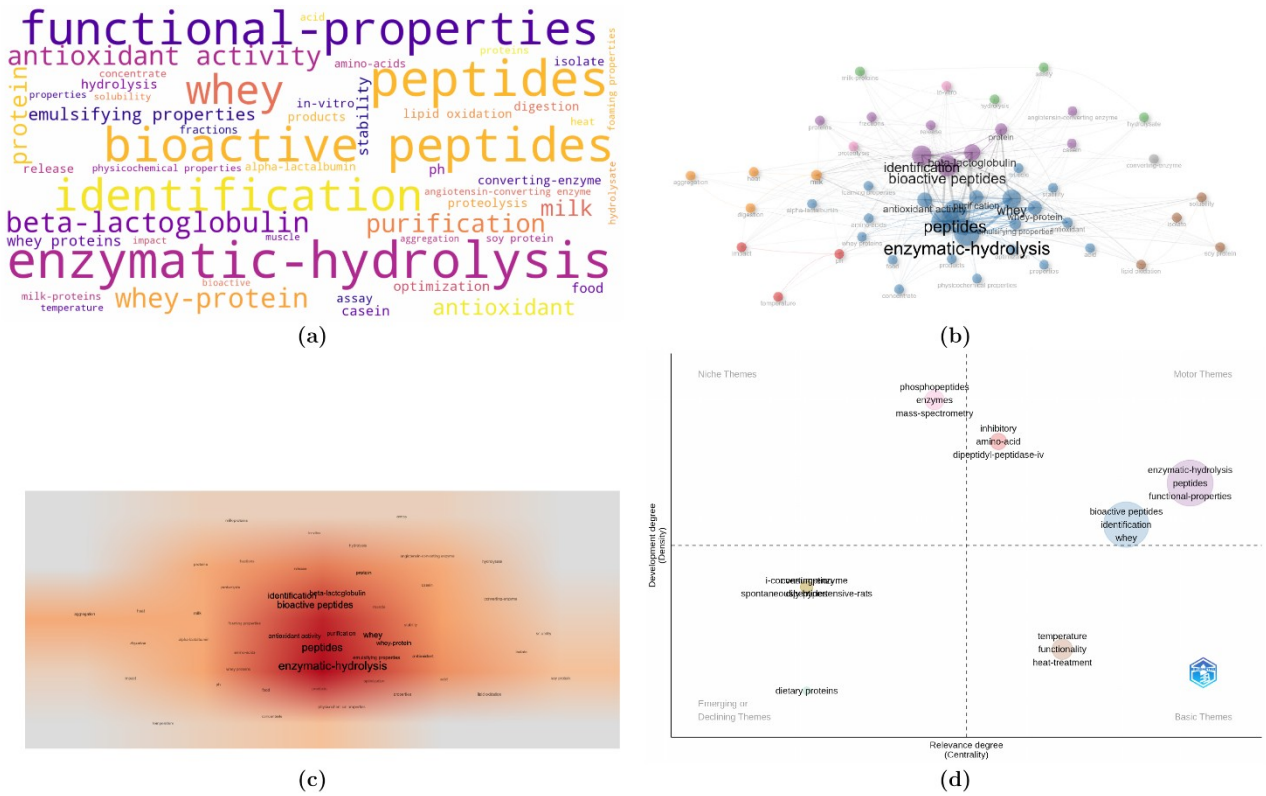

Fig. 2 Authors’ keywords analysis related to enzymatic hydrolysis of bovine whey and its bioactive peptides: (a) Word cloud, (b) Co-occurrence network diagram, (c) Density map, and (d) Thematic map.

Fig. 2d presented a thematic map, categorizing various research themes based on their development degree (density) and relevance degree (centrality) within the enzymatic hydrolysis of bovine whey and its bioactive peptides. The map was divided into four quadrants: Motor Themes, Basic Themes, Niche Themes, and Emerging or Declining Themes.

In the Motor Themes quadrant, which featured topics that were both highly developed and central to the field, terms such as “enzymatic hydrolysis”, “peptides”, and “functional properties” were prominent. These themes represented the core focus of the research, driving significant advancements in understanding the functional characteristics of whey-derived bioactive peptides. Their high centrality and density indicated that these topics were well-established and likely to continue being influential in the field.

The Basic Themes quadrant included terms like “bioactive peptides”, “identification”, and “whey”. Although these topics were central to the research, they had a lower density, suggesting that while they were foundational to the field, they might require further development to explore their potential fully. These themes formed the backbone of the research, providing essential insights that supported more advanced studies.

In the Niche Themes quadrant, themes such as “phosphopeptides”, “enzymes”, and “mass spectrometry” were identified. These topics were highly developed but less central to the overall research landscape. This placement suggested that these areas were specialized and well-researched but not as broadly influential. They might represent areas of concentrated expertise or emerging specialties within the broader context of whey protein research.

The Emerging or Declining Themes quadrant included terms such as “dietary proteins”, “i-converting enzyme”, and “spontaneously hypertensive rats”. These topics had low centrality and density, indicating either emerging areas of research that had not yet gained prominence or declining areas that were losing relevance. These themes in this quadrant suggested they might represent exploratory research directions or areas where interest was waning.

These visualizations effectively summarized the key topics, themes, and relationships within the literature on enzymatic hydrolysis of bovine whey and bioactive peptides. The word cloud provided a quick, yet comprehensive overview of dominant research focuses. At the same time, the co-occurrence network and density map highlighted the interconnectedness of terms and the structure of the research field. Identifying key clusters, such as “enzymatic-hydrolysis” and “bioactive peptides”, underscored the primary research directions driving the study area. Finally, the thematic map offered a detailed view of the research landscape, emphasizing both established and emerging themes and providing valuable insights into the current state of the field and potential areas for future exploration.

3.3. Factorial analysis

Fig. 3 presents the conceptual structure map generated using the Multiple Correspondence Analysis (MCA) method based on the dataset obtained with the specified logical equation. The map revealed key thematic clusters within the research on the enzymatic hydrolysis of bovine whey and its bioactive peptides with functional properties.

A central cluster was identified around “enzymatic hydrolysis”, “peptides”, and “functional properties”, which were closely associated with terms such as “whey”, “whey protein”, and “bioactive peptides”. These findings suggested that the core research focus in this field was centered on the hydrolysis process and the identification and optimization of peptides with bioactive properties.

Significant terms like “digestion”, “pH”, and “proteins” were positioned toward the right side of the map, indicating their relevance in studies focusing on the physicochemical and digestive aspects of whey proteins and peptides. Additionally, terms related to antioxidant properties, such as “oxidative stress” and “antioxidant activity”, were clustered, pointing to a distinct research interest in the health benefits of these peptides. The peripheral positioning of terms like “soy protein”, “solubility”, and “lipid oxidation” indicated that these topics were less emphasized within the dataset, suggesting potential areas for further exploration.

The MCA map effectively summarized the conceptual structure of the research field, highlighting the central themes and emerging areas of study. It also provided valuable insights into the relationships between key topics in the literature on enzymatic hydrolysis of bovine whey and bioactive peptides.

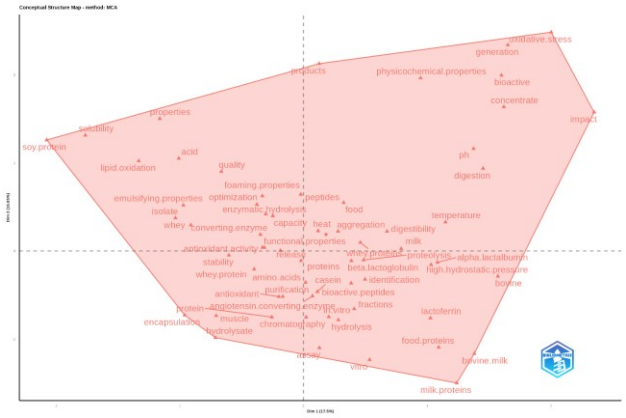

Fig. 3 Conceptual structure map of research on enzymatic hydrolysis of bovine whey and bioactive peptides.

3.4. Future directions

The findings of this study are significant as they advance the understanding of the functional properties of whey-derived peptides, such as antioxidant and antihypertensive effects, and their potential applications in the food and pharmaceutical industries, promoting innovation and sustainability.

Recent studies have underscored the development of novel technologies to optimize the production of bioactive peptides from bovine serum. For instance, ultrasound-assisted enzymatic hydrolysis has significantly enhanced the hydrolysis process’s efficiency and the resulting peptides’ biological activity (Qian et al., 2023). Integrated approaches combining enzyme selection, substrate pretreatment, and bioprocessing technologies have also improved enzymatic hydrolysis efficiency, with potential applications for bovine serum (Pandey & Agrawal, 2024). These innovations not only increase yield but also offer more sustainable processing options.

International collaborations have been crucial in advancing bioactive peptide research by facilitating the sharing of knowledge and resources, leading to innovative solutions and improved research outcomes. For example, initiatives focused on sustainable biopharmaceutical production have strengthened partnerships between academia and industry, fostering the development of greener peptide synthesis processes (Ferrazzano et al., 2022; Koenig et al., 2018). Such collaborations can be instrumental in addressing global challenges in peptide production and application.

Despite bioactive peptides’ promising potential, commercialization faces regulatory hurdles, production scalability, and cost-effectiveness (Isidro-Llobet et al., 2019). However, these barriers can be overcome through innovative production methods and exploring new markets for peptide applications (Jadhav et al., 2021). Integrating sustainable practices in peptide production can also enhance market acceptance and consumer interest. Sustainability remains a critical focus in bioactive peptide production. Utilizing food industry by-products like bovine serum contributes to a circular economy by reducing waste and environmental impact (Carrera-Alvarado et al., 2023; Pratama et al., 2022). Additionally, microbial fermentation and enzymatic process advancements offer more sustainable pathways for peptide production, aligning with global sustainability goals (Chaudhary et al., 2024; Lübeck & Lübeck, 2022).

Looking forward, bioactive peptide research is expected to grow significantly, with emerging interests in novel peptide sources like marine by-products and advanced delivery systems for peptide therapeutics (Pratama et al., 2022; Pratap-Singh et al., 2023). Continued research into peptide functional properties will likely reveal new applications and health benefits, expanding their relevance in the food and pharmaceutical sectors (Jakubczyk et al., 2020).

The enzymatic hydrolysis of bovine serum presents numerous opportunities for producing bioactive peptides with diverse applications. The field can progress toward more sustainable and effective peptide production by addressing challenges, leveraging technological innovations, and fostering international collaboration.

4. Concluding remarks and perspectives

The comprehensive analysis of the global food science and technology research landscape from 2004 to 2024 underscores the significant contributions from countries such as China, Canada, India, and Brazil. Key journals like “LWT-Food Science and Technology” and “Food Chemistry” have been pivotal in disseminating influential research, particularly in the enzymatic hydrolysis of whey proteins.

Noteworthy studies by Mohammadian and Madadlou (2016) and Cotabarren et al. (2019) have emerged as highly cited works, reflecting the centrality of themes such as “enzymatic hydrolysis”, “peptides” and “bioactive peptides” in the field. The thematic map analysis further categorizes research into motor, essential, niche, and emerging or declining themes, highlighting food science research’s dynamic and interdisciplinary nature. The study also reveals a robust growth in scientific production, with a 12.74% annual increase in publications and a robust collaborative environment, as evidenced by an average of 4.92 co-authors per paper and significant international collaborations.

The research on enzymatic hydrolysis of bovine whey and its bioactive peptides presents promising avenues for further exploration. The identified functional properties, such as antioxidant, antihypertensive, antidiabetic, antithrombotic, and hypocholesterolemic effects, suggest substantial potential for applications in food and pharmaceutical industries. Future research should optimize production technologies, explore novel applications, and address existing gaps, particularly in emerging themes like dietary proteins. Continued interdisciplinary collaboration and international partnerships will be crucial in advancing the understanding and utilization of whey-derived peptides, ultimately contributing to improved health outcomes and innovative food solutions.

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Authors' Contributions

L.G.-C. and E.P.-E.: Conceptualization; J.G.P.-F. and I.R.-R.: Data curation; E.C.-L. and I.R.-R.: Formal analysis; L.G.G.-O. and I.R.-R.: Investigation; J.G.P.-F. and L.G.-C.: Methodology; J.G.P.-F.: Software; E.P.-E. and L.B.O.-R.: Supervision; L.G.G.-O. and L.B.O.-R: Validation; E.P.-E. and E.C.-L.: Visualization; J.G.P.-F. and I.R.-R.: Writing - original draft; E.P.-E.: Writing – review & editing. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no competing interests.

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