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Review article

Innovative treatments for obesity and NAFLD: A bibliometric study on antioxidants, herbs, phytochemicals, and natural compounds

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ABSTRACT

The increasing scientific interest in antioxidants and naturally derived compounds as potential remedies for obesity and non-alcoholic fatty liver disease (NAFLD) has led to extensive research. The objective of this bibliometric analysis is to present an updated perspective on the topic of antioxidants, herbs, phytochemicals, and natural compounds, in the control of obesity and NAFLD, to identify new areas for future research. Publications from the years 2012–2022 were retrieved using the Scopus database. The research trends were analyzed using the Biblioshiny and VOSviewer tools. The field has seen a significant increase in research activity, as indicated by an annual growth rate of 10 % in the number of published manuscripts. China, Korea, and the USA emerged as the most prominent contributors in this specific field, supported by their notable volumes of publications and citations. The density analysis revealed that the most frequently occurring authors' keywords related to herbal species are, in rank order*, Camelia sinensis, Momordica charantia, Curcuma longa, Ilex paraguariensis, Panax ginseng, Moringa oleifera, Garcinia cambogia, Garcinia mangostana, Zingiber officinale, and Cinnamomum verum.* In the group of antioxidants, phytochemicals, and natural compounds, the top 10 were resveratrol, curcumin, quercetin, vitamin E, alpha-lipoic acid, vitamin C, chlorogenic acid, lycopene, fucoxanthin, and berberine. The co-occurrence analysis unveiled significant themes and potential trends, including a notable interest in the impact of herbal species, antioxidants, phytochemicals, and natural compounds on obesity and NAFLD through the modulation of the gut microbiome. Another recurring theme that arises, is the ongoing investigation of molecular targets that demonstrate anti-adipogenesis properties. The analysis presented in this study provides valuable insights for researchers investigating the efficacy of antioxidants, herbs, phytochemicals, and natural compounds in addressing obesity and NAFLD. Through the use of bibliometric methods, the study offers a comprehensive overview. Furthermore, the findings of this analysis can serve as a foundation for future research in this specific domain.

1. Introduction

The global incidence of obesity has experienced a nearly threefold rise over the last three decades [1,2]. Obesity is a pathological

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condition that impacts individuals across various age groups, ethnicities, and economic statuses [1,3,4] and is characterized by excessive adipose tissue accumulation due to inadequate energy expenditure [3,5]. Obesity is linked to a range of negative health consequences, including but not limited to coronary heart disease, type 2 diabetes mellitus, high blood pressure, stroke, abnormal lipid profiles, osteoarthritis, and sleep apnea [6–9]. Obesity-induced inflammation and insulin resistance contribute to the development of neurodegenerative diseases by disrupting brain homeostasis, leading to cognitive decline and neurodegeneration [10,11]. Furthermore, there is strong evidence that obesity is associated with non-alcoholic fatty liver disease (NAFLD) [8,12,13]. According to epidemiological studies, there is a positive correlation between being overweight and the incidence of NAFLD. The prevalence of NAFLD ranges from 22.5 % to 44.0 % in overweight individuals, while in obese individuals it can be as high as 90 % [8,12,13]. Notably, NAFLD is a medical condition characterized by the accumulation of lipids within hepatocytes, which occurs independently of alcohol consumption. NAFLD encompasses a diverse spectrum of liver injuries, ranging from simple accumulation of fat in the liver (steatosis) to non-alcoholic steatohepatitis, which is characterized by histological evidence of hepatocyte damage, inflammation, and variable degrees of fibrosis [14–17]. The majority of these pathological states are commonly linked with obesity or excessive weight, which are established risk factors for the initiation of NAFLD [15,18,19].

The complex origins of obesity and NAFLD, involving various factors such as environmental, psychological, genetic, and physiological determinants, present considerable obstacles to the successful treatment, control, and avoidance of this disorder [20,21]. Regarding obesity, numerous investigations have been conducted regarding anti-obesity drugs as a feasible therapeutic strategy for managing obesity [22]. Despite the pharmacological effects of medications, they often have the potential to cause harmful adverse reactions [23,24]. Currently, there is no established pharmacological intervention for NAFLD, as its pathogenesis remains poorly understood [25,26]. The primary approach for managing this condition involves lifestyle modifications, such as dietary adjustments and exercise, to facilitate weight loss [25,26].

Scientists are becoming more interested in using antioxidants, phytochemicals, and compounds from natural sources to treat diseases like obesity and NAFLD. This has led to a lot of research, and many studies have been done to look at the positive and negative effects of these medicines [27–32].

Bibliometric analysis is a methodical and quantitative approach that utilizes mathematical and statistical methods to assess the interconnectedness and impact of publications within a particular research field [33]. An advantage of this methodology is its ability to provide a complete viewpoint on numerous pieces of academic literature, facilitating the expedient recognition of noteworthy research [33]. Currently, there are a limited number of bibliometric studies relative to the utilization of antioxidants, phytochemicals, or herbal remedies for the treatment of obesity. For example, a bibliometric analysis was recently conducted to comprehensively analyze research on herbal medicine for obesity over the past 20 years [34]. As regards NAFLD, there are no bibliometric studies specifically focused on the relationship between antioxidants, phytochemicals, and/or herbs and the disease.

Previous bibliometric analyses have investigated emerging patterns and focal points in the fields of metabolic-dysfunction-associated fatty liver disease (MALD) and the relationship between gut microbiota and MALD, utilizing the Web of Science database [35,36]. In an attempt to gain a deeper understanding of the involvement of the gut-liver axis in NAFLD, Yang et al. undertook a comprehensive examination of worldwide publication trends and areas of concentrated research [37].

Recently, our research group conducted a bibliometric study to specifically evaluate recent publishing trends from 2002 to 2022 concerning the relationships between the gut microbiome, all stages of liver disease, from NAFLD to cirrhosis, and their connections with biotics (prebiotics, probiotics, symbiotics, postbiotics, and parabiotics) [38].

Different from our previous study, the purpose of this bibliometric analysis is to specifically evaluate recent publishing trends from 2012 to 2022 to track the evolution of knowledge regarding the use of antioxidants, herbs, phytochemicals, and natural compounds in the treatment of obesity and NAFLD. The purpose was to identify new areas for future research and provide an updated perspective on the topic.

2. Methods

We performed a comprehensive literature search using the electronic Scopus database [39,40]. Scopus uniquely combines a comprehensive, expertly curated abstract and citation database with enriched data and linked scholarly literature across a wide variety of disciplines [39,40]. We used the appropriate keywords to identify relevant literature from 2012 to 2022 on the role of antioxidants, herbs, phytochemicals and natural compounds in the management of obesity and NAFLD. To prevent bias caused by continuous database modifications, the extraction and export of documents should be completed within one day. The search was limited to original articles written in English. The date of the retrieval was April 17, 2023. The research string used was the following query: TITLE-ABS-KEY (((obesity) OR (nafld) OR ("non-alcoholic fatty liver disease") OR ("nonalcoholic fatty liver disease") OR ("non alcoholic fatty liver disease")) AND ((antioxid*) OR (anti-oxid*) OR (herb*) OR ("natural compoun*") OR ("natural produc*") OR (phytochemica*) OR (extract))) AND PUBYEAR > 2011 AND PUBYEAR < 2023 AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (LANGUAGE, "English")). Data mining was performed on the title, abstract and keywords. By thoroughly examining the retrieved publications, we verified the efficacy of our search strategy. Bibliometric analyses were performed using the Bibliometrix and Biblioshiny tools and the VOSviewer software [41]. Bibliometrix is an R package containing a series of functions for scientometric quantitative research [41]. The Bibliometrix R package was installed and subsequently loaded into R Studio (vers. 022.12.0+353). The Biblioshiny application was initiated by executing the command Biblioshiny in the R console [41]. Biblioshiny is a web-based software tool that facilitates the utilization of the Bibliometrix package of the R programming language [41]. The bibliographic data set was obtained in "CSV" format from the Scopus database and uploaded to the Biblioshiny interface. Bibliometrix and Biblioshiny tools were used in conjunction with the software VOSviewer (version 1.6.19) to perform the processing and map visualization of the literature data retrieved.

3. Results

3.1. Publication trends and most productive sources

Based on the parameters of the search, 12557 articles covering the years 2012–2022 were retrieved from the Scopus database. Over the past decade, the number of publications in this sector has increased rapidly (Fig. 1), demonstrating that antioxidants, herbs, phytochemicals, and natural compounds for obesity and NAFLD have gained worldwide attention. Since 2012, there has been a constant growth rate of about 10 % per year.

Fig. 2 presents a ranking of the twenty most prolific journals concerning both publications (A) and citations (B) pertaining to the researched field. The top five journals with the highest number of publications, listed in descending order, are *Nutrients* (published by MDPI, Multidisciplinary Digital Publishing Institute), *Food and Functions* (published by the Royal Society of Chemistry), *PLOS One* (published by the Public Library of Science), *Molecules* (published by MDPI), and *Evidence-Based Complementary and Alternative Medicine* (published by Hindawi Publishing Corporation). In terms of citations, the journals *Nutrients*, *PLOS* One, and *Food and Function* dominate the ranking, but in this case, the journal *Food and Function* goes down to third place, followed by the *Journal of Nutritional Biochemistry* (published by Elsevier) and the *Journal of Agricultural and Food Chemistry* (published by the American Chemical Society). The journals *Molecules* and *Evidence-Based Complementary and Alternative Medicine* have been ranked fourteenth and sixteenth, respectively, in the citation ranking. Approximately 43 % of all retrieved documents were comprised of 5478 articles published in the top 20 journals.

As shown in Table 1, the analysis of the trend in the publication of each of the 20 most productive journals reveals that some journals have had a growing interest in the field in the last 10 years. Six journals will see an increase in the number of articles from 2021 to 2022. The journal with the greatest increase is the *Journal of Nutritional Biochemistry*, with 32 more articles than in 2021 (+60 %), followed by *Nutrients* with 32 articles (+40 %), and *Antioxidants* with 12 articles (+33.4 %). Three of the 20 most productive journals do not have an increase, while the remaining 11 journals have an annual reduction in articles from 2021.

The visualization presented in Fig. 3 depicts a bibliometric coupling network map of journals, wherein only those journals that have contributed a minimum of 25 articles have been considered. The map analysis reveals the existence of four clusters. Each cluster denoted a group of journals that exhibited a comparable citation pattern. In the red cluster, most journals were bibliographically coupled with the *Journal of Nutritional Biochemistry*, *Journal of Medicinal Food*, and *PLOS One*, while in the green cluster, most journals were bibliographically coupled with the *Food and Function* and *Journal of Agricultural and Food Chemistry* journals. In the yellow cluster, most journals were bibliographically coupled with the *Journal of Medicinal Food* and *Evidence-Based Complementary and Alternative Medicine* journals. In the blue cluster, most journals were bibliographically coupled with *Nutrients*, *Antioxidants*, and the *International Journal of Molecular Sciences*.

3.2. Most productive/influential countries and institutions

From 2012 to 2022, research papers pertaining to the field were distributed across 211 distinct countries. The scientific output of various nations in terms of publications and cross-national cooperation in the field has been depicted in Fig. 4A. SCP indicates Single-Country Publications, while MCP refers to Multiple-Country Publications. The data reveals that China, Korea, and the USA have respectively produced 2318, 1460, and 1023 publications. International collaboration was involved in obtaining 356 articles from

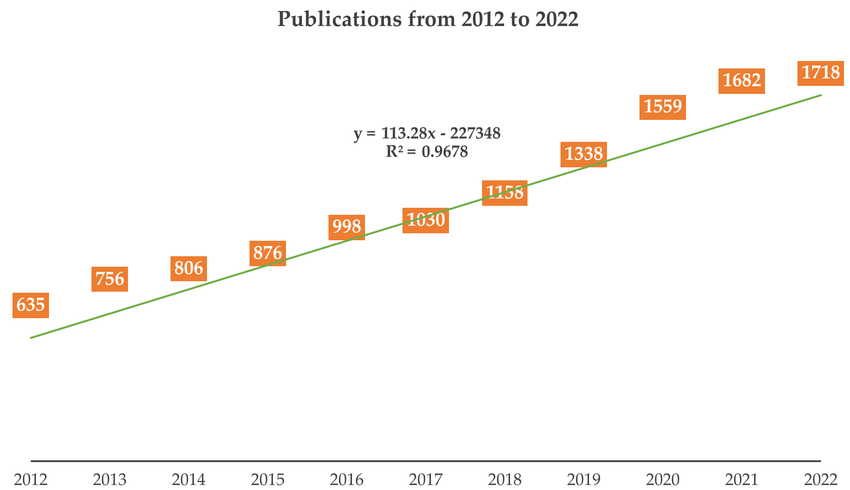

Fig. 1. The number of publications between 2012 and 2022. All numbers are derived from Scopus on April 17, 2023.

Fig. 2. List of the 20 most productive journals in terms of publications (A) and citations (B), in descending order. All numbers are derived from Scopus on April 17, 2023.

China. The nations exhibiting a substantial number of global partnerships are the USA, Korea, and China. Nonetheless, it is possible to make certain observations pertaining to the MCP ratio of the leading ten nations, specifically in relation to the overall quantity of publications. Spain exhibits the highest MCP ratio at 37 %, followed by Italy (35 %) and the USA (33 %). In the meantime, it is noteworthy that nations like Spain and Italy exhibit a comparatively elevated count of SCP in contrast to MCP. The countries with the highest number of citations in the research field are depicted in Fig. 4B. The presented data indicate that China holds the foremost position in this particular area of research, with the USA and Korea following closely behind. These nations hold significant influence due to their substantial contributions to research publications in this particular field. Notably, Spain, Japan, India, and Italy exhibit a substantial average citation rate, indicating that they have garnered a considerable number of citations relative to their published articles.

The visual representation presented in Fig. 5 illustrates the top 50 nations that hold the highest co-authorship value. The analysis of co-authorship among nations provides insight into the extent and nature of collaborative efforts within a given field. The network comprises nodes that correspond to distinct countries, while the edges that connect these nodes signify the level of collaboration between the respective countries. The size of the country represents the frequency with which this country collaborates, and the thickness of an edge indicates the proximity of the collaboration between countries. The items are clustered based on their respective colors. There are four distinct clusters or communities present in the network, each of which has a distinctive node color. According to this map, China collaborates closely with Australia, Malaysia, Saudi Arabia, Iran, and Korea, which in turn collaborate directly with Hong Kong, Indonesia, Iraq, and Thailand. The USA engaged closely with Japan and Sweden in the green cluster, but it also established a bridge of partnerships with China. The red- and violet-colored clusters are made up of countries that are mostly from the Eurozone but also include the UK, Brazil, Argentina, and Chile.

Table 2 presents a comprehensive list of the top 10 institutions that have conducted research on the utilization of natural antioxidants, herbs, phytochemicals, and natural compounds in the management of obesity and NAFLD, ranked according to the number of publications they have produced on the subject matter. The Shanghai University of Traditional Chinese Medicine (China) and Kyung Hee University (South Korea) are the two most productive institutions in terms of publication output, with 610 and 596 documents

Table 1
Publication trend of the 20 most prolific journals relative to the last 10 years.

		2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	% var. from 2021 to 2022
Nutrients	PY	1	6	10	13	16	43	64	95	115	80	112	+40,0
	CMT	1	7	17	30	46	89	153	248	363	443	555	
Plos One	PY	16	31	36	25	25	24	20	16	9	8	10	+25,0
	CMT	16	47	83	108	133	157	177	193	202	210	220	
International Journal of Molecular Sciences	PY	4	4	6	1	2	9	27	29	32	28	34	+21,5
	CMT	4	8	14	15	17	26	53	82	114	142	176	
Journal of Food Biochemistry	PY	0	1	1	2	3	7	8	15	24	20	32	+60,0
	CMT	0	1	2	4	7	14	22	37	61	81	113	
Frontiers in Pharmacology	PY	0	0	1	1	5	9	10	13	16	25	33	+32,0
	CMT	0	0	1	2	7	16	26	39	55	80	113	
Antioxidants	PY	0	0	0	0	0	0	1	22	46	36	48	+33,4
	CMT	0	0	0	0	0	0	1	23	69	105	153	
Phytomedicine	PY	12	5	5	3	3	4	8	11	16	15	15	0,0
	CMT	12	17	22	25	28	32	40	51	67	82	97	
Jounal of Functional Foods	PY	3	5	15	17	13	21	14	24	19	15	15	0,0
	CMT	3	8	23	40	53	74	88	112	131	146	161	
BMC Complementary and Alternative Medicine	PY	3	8	11	13	16	20	11	18	0	0	0	0,0
	CMT	3	11	22	35	51	71	82	100	100	100	100	
Food and Function	PY	2	5	14	22	15	18	24	34	26	47	41	−12,8
	CMT	2	7	21	43	58	76	100	134	160	207	248	
Molecules	PY	3	6	7	5	13	11	18	25	29	49	40	−18,4
	CMT	3	9	16	21	34	45	63	88	117	166	206	
Evidence-Based Compl. and Alternative Medicine	PY	14	34	7	17	11	15	21	13	18	29	16	−44,8
	CMT	14	48	55	72	83	98	119	132	150	179	195	
Journal of Ethnopharmacology	PY	8	7	14	15	23	9	8	18	31	30	26	−13,3
	CMT	8	15	29	44	67	76	84	102	133	163	189	
Biomedical and Pharmacology	PY	0	0	0	0	9	31	34	26	21	39	22	−43,6
	CMT	0	0	0	0	9	40	74	100	121	160	182	
Journal of Medicinal Food	PY	7	6	13	15	21	18	15	18	23	12	9	−25,0
	CMT	7	13	26	41	62	80	95	113	136	148	157	
Scientific Reports	PY	0	1	4	6	19	20	16	15	23	18	13	−27,8
	CMT	0	1	5	11	30	50	66	81	104	122	135	
Journal of Nutritional Biochemistry	PY	11	11	6	8	14	13	17	9	17	15	8	−46,7
	CMT	11	22	28	36	50	63	80	89	106	121	129	
Journal of Agricultural and Food Chemistry	PY	11	8	8	13	7	10	13	18	17	10	8	−20,0
	CMT	11	19	27	40	47	57	70	88	105	115	123	
Oxidative Medicine and Cellular Longevity	PY	0	4	5	4	10	12	16	11	13	19	11	−42,1
	CMT	0	4	9	13	23	35	51	62	75	94	105	
Phytotherapy Research	PY	14	11	5	4	8	7	5	11	7	22	5	−77,3
	CMT	14	25	30	34	42	49	54	65	72	94	99	

PY=Per year; CMT = cumulative. In the last column is indicated the % of variation relative to the number of articles from 2021 to 2022. All numbers are derived from Scopus on April 17, 2023.

respectively. The Beijing University of Chinese Medicine (China) and Huazhong University of Science and Technology (China) have published a similar number of articles, with 330 and 314 publications, respectively. Kyungpook National University (South Korea), Tehran University of Medical Sciences (Iran), and China Pharmaceutical University (China) form a group of institutions that exhibit a similar quantity of scholarly articles. Similarly, the institutions of Universitat Rovira I Virgili (Spain), Seoul National University (South Korea), and the Korea Institute of Oriental Medicine (South Korea) also constitute a cluster of institutes with a comparable number of publications.

The examination of trend publications resulting from the top 10 most prolific institutions (Fig. 6) indicates that Shanghai University of Traditional Chinese Medicine and Kyung Hee University have exhibited a notable increase in growth in comparison to their counterparts.

The institutions with the highest co-authorship value are depicted in Fig. 7. The co-authorship analysis demonstrates the extent of collaboration as well as the collaboration between institutions in this field. The network's nodes represent institutions, while the edges connecting them indicate collaboration between institutions. The size of a node represents the frequency with which this institution collaborates, while the thickness of an edge shows the proximity of collaboration. Colors represent how the objects are grouped together. The network contains six major clusters or communities, each with a different node color, interconnected with each other.

3.3. Most cited paper

The measurement of citations provides a significant metric for assessing the influence of a scholarly article within a particular field of research. The relevant literature specific to antioxidants, herbs, phytochemicals and natural compounds for the cure of obesity and NAFLD was extracted and subsequently, the top 20 most cited original papers were presented in Table 3.

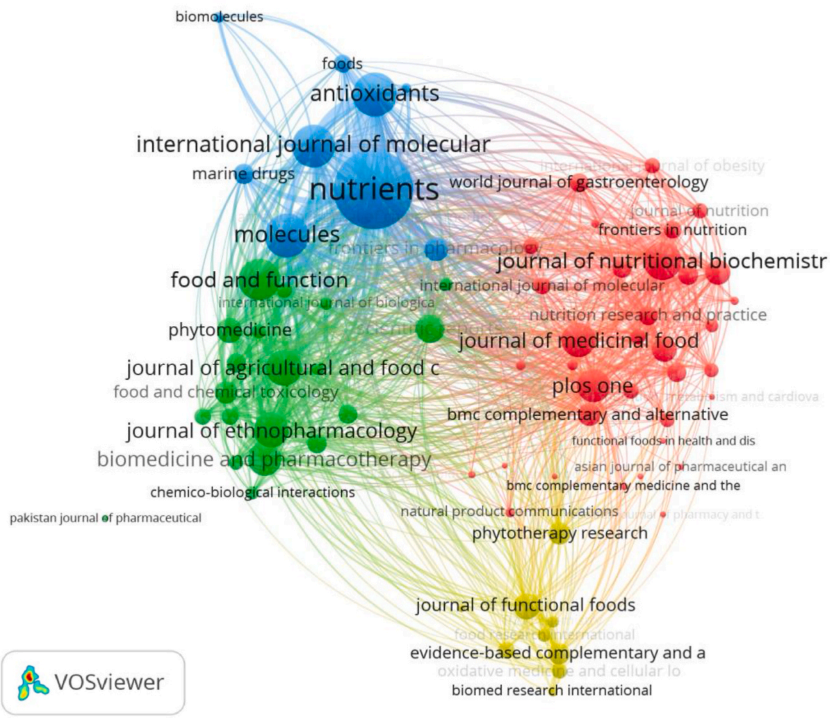

Fig. 3. Visualization map of bibliometric coupling of journals based on source link-weights and with a minimum contribution of 25 articles. Each cluster represented journals with a similar citation pattern. All numbers are derived from Scopus on April 17, 2023.

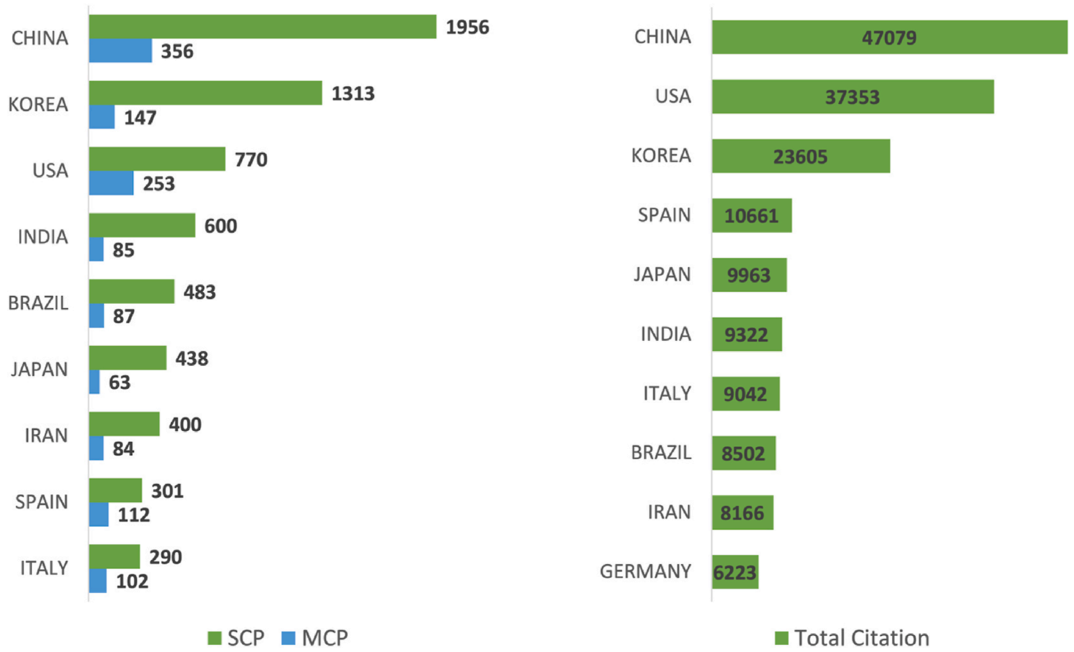

Fig. 4. The top 10 most productive countries in terms of publications (A) and citations (B), in descending order for Single Country Publications and citations (SCP) and number of citations. MCP = Multi Country Publications. All numbers are derived from Scopus on April 17, 2023 and are elaborated by Biblioshiny.

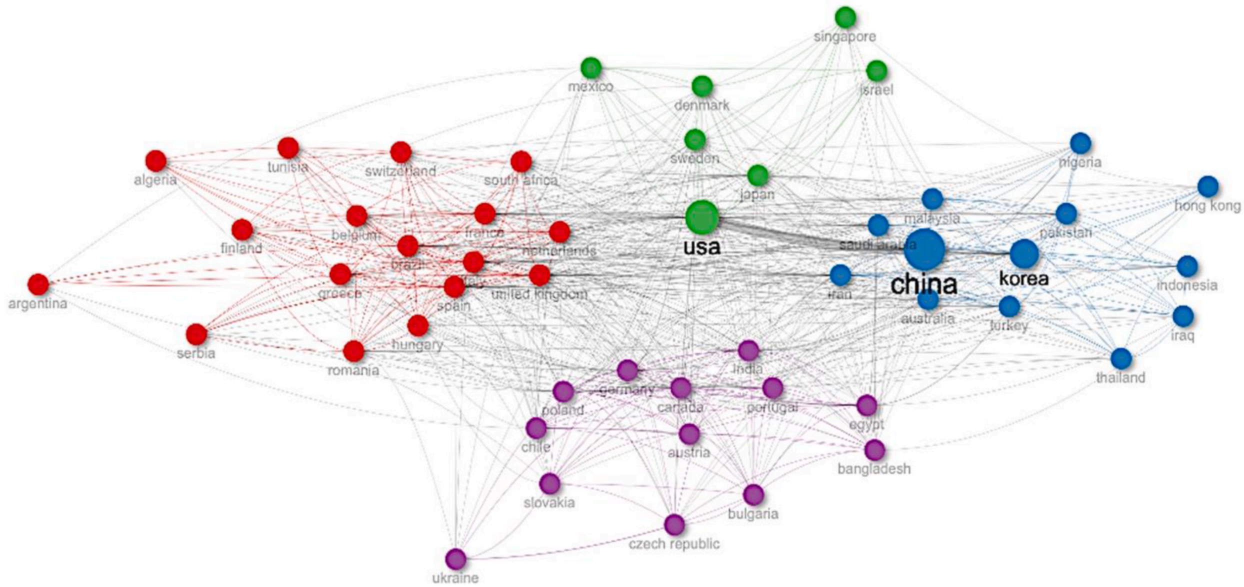

Fig. 5. Network of country coauthorship map, weighted by the total link strength, representing 4 clusters of collaborations. Included countries (N = 50). All numbers are derived from Scopus on April 17, 2023. This network was generated by Biblioshiny.

Table 2
Top ten institution productivity.

Institution	Articles
Shanghai University of Traditional Chinese Medicine	610
Kyung Hee University	596
Beijing University of Chinese Medicine	330
Huazhong University of Science and Technology	314
Kyungpook National University	290
Tehran University of Medical Sciences	287
China Pharmaceutical University	280
Universitat Rovira I Virgili	262
Seoul National University	260
Korea Institute of Oriental Medicine	257

All numbers are derived from Scopus on April 17, 2023 and elaborated by Biblioshiny.

The paper authored by Chang et al. [42] has the highest number of citations. Despite focusing on the medicinal properties of a mushroom, which belongs to a distinct kingdom known as the "mushroom kingdom" rather than the higher plant kingdom, it is a noteworthy study that we considered worthy of inclusion together with the paper by Wu et al. [43]. The conditions of obesity and NAFLD have been found to be linked with persistent low-level inflammation and intestinal dysbiosis [44,45]. In an experimental study conducted on mice that were fed a high-fat diet, Chang et al. [42] observed that the administration of water extract of *Ganoderma lucidum* mycelium (WEGL) resulted in a reduction in body weight, inflammation, and insulin resistance. The findings suggest that WEGL has the potential to mitigate the negative effects of HFD-induced gut dysbiosis, including a reduction in *Firmicutes-to-Bacteroidetes* ratios and levels of *Proteobacteria* carrying endotoxins. WEGL appears to preserve the integrity of the intestinal barrier and decrease metabolic endotoxemia. They demonstrated that the anti-obesity and microbiota-modulating properties could be transmitted through horizontal faeces transfer from mice treated with WEGL to mice fed with HFD. Additionally, the researchers found that high molecular weight polysaccharides extracted from WEGL produce comparable anti-obesity and microbiota-modulating effects. Instead, the study conducted by Wu et al. [43] revealed that the anti-obesity effects of polysaccharides derived from Hirsutella sinensis are primarily mediated by the intestinal commensal *Parabacteroides goldsteinii*. The administration of live *P. goldsteinii* to mice fed with a high-fat diet resulted in a decrease in obesity. This was accompanied by increased thermogenesis in adipose tissue, improved intestinal integrity, and reduced inflammation and insulin resistance.

Studies have demonstrated the potential of plant extracts and natural compounds to mitigate gut dysbiosis. In a study conducted by Anhê et al. [46], it was shown that a polyphenol-rich extract derived from *Vaccinium macrocarpon* has the potential to safeguard against diet-induced obesity, insulin resistance, and intestinal inflammation. This effect was observed in mice and was found to be associated with an increase in the population of *Akkermansia* spp. in the gut microbiota. There is a mounting body of evidence suggesting that a higher prevalence of *Akkermansia* spp. in the intestines may serve as a protective measure against the metabolic syndrome associated

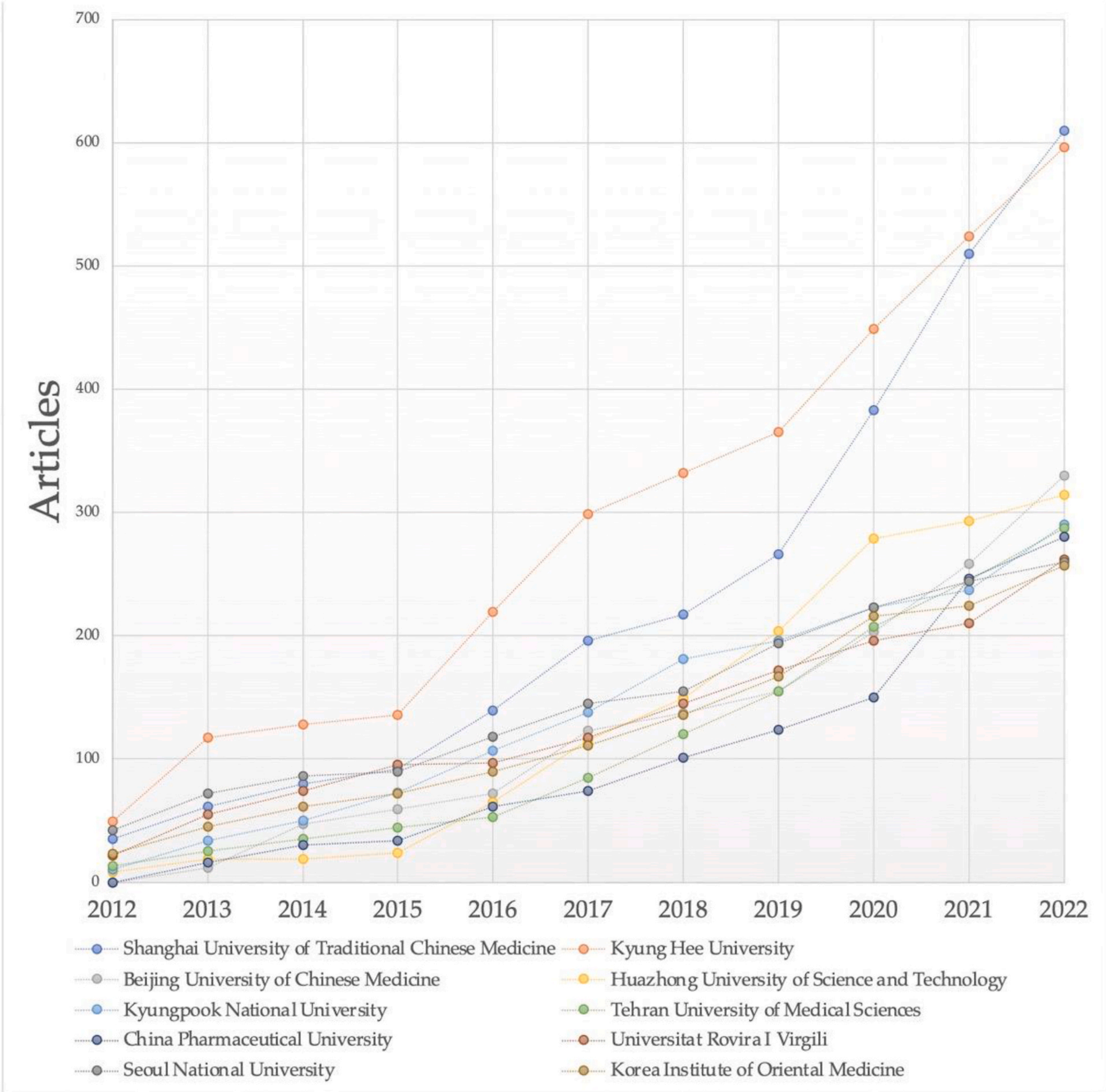

Fig. 6. Top-ten institution's production over time. All numbers are derived from Scopus on April 17, 2023.

with obesity [47].

In their paper, Zhang X et al. [48] found that berberine has been found to be efficacious in preventing the onset of obesity and insulin resistance in rats that were fed a high-fat diet. This effect is believed to be, at least in part, due to the structural modification of the gut microbiota, which may aid in reducing inflammation by decreasing the exogenous antigen load in the host and increasing the levels of short-chain fatty acids in the intestine [48]. Berberine also boosts energy expenditure, restricts weight gain, improves cold tolerance, and promotes brown adipose tissue activity in obese *db/db* mice, as Zhang Z et al. reported [49]. The flavonoid quercetin has also been shown to have a protective effect in a nutritional animal model of NAFLD associated with obesity, and its activity is mediated by modulating intestinal microbiota imbalance and related gut-liver axis activation, as demonstrated in a paper published in 2017 by Porras et al. [50].

The third article cited is by Liu et al. [51], reported that Celastrol, a pentacyclic triterpene derived from the roots of the *Tripterygium wilfordi* plant, is an effective anti-obesity drug. Celastrol lowers food intake, prevents energy expenditure decline, and leads to up to 45 % weight loss in hyperleptinemic diet-induced obese mice by boosting leptin sensitivity; however, it is ineffective in leptin-deficient (*ob/ob*) and leptin receptor-deficient (*db/db*) mouse models. Celastrol is a leptin sensitizer and a prospective drug for the pharmacological treatment of obesity, according to these findings.

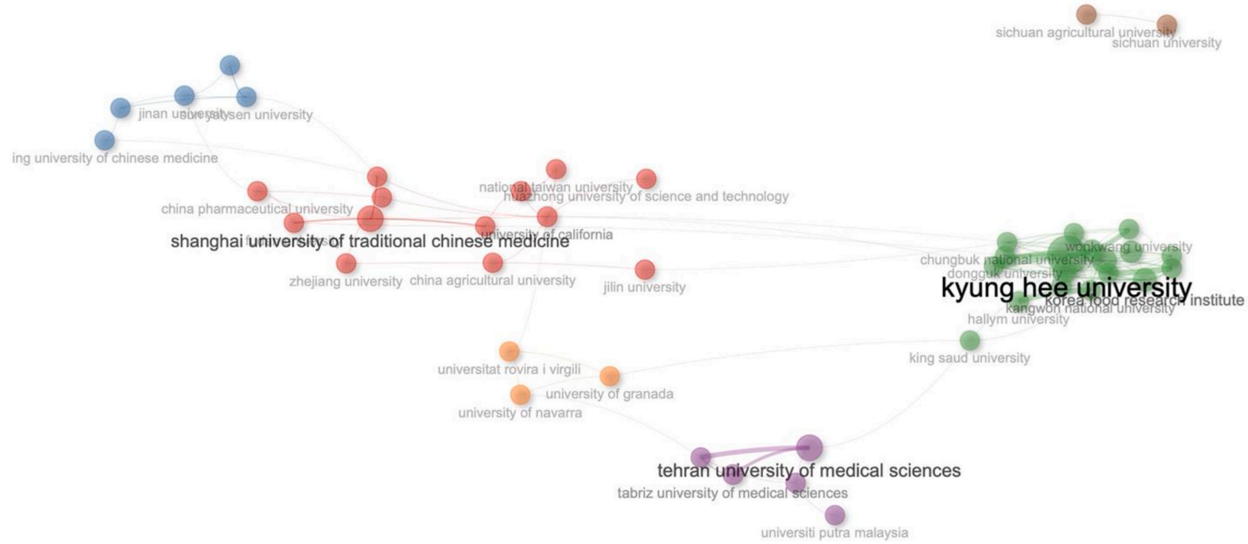

Fig. 7. Network of institutions coauthorship map, weighted by the total link strength, representing 10 clusters of collaborations. All numbers are derived from Scopus on April 17, 2023. This network was generated by Biblioshiny.

A number of studies ranked among the top 20 have reported the advantageous impacts of resveratrol on obesity [52] and NAFLD [53]. However, there is conflicting data on this matter [54,55]. The study conducted by Chachay et al. revealed that the administration of resveratrol (3000 mg/day) for a duration of eight weeks did not exhibit any significant improvement in the characteristics of NAFLD in comparison to the placebo group. The study consisted of 20 participants, with 10 receiving a placebo and the remaining 10 receiving resveratrol. In a study conducted by Poulsen et al. [54], it was observed that the administration of resveratrol (1000 mg/day) for a duration of four weeks did not result in any significant changes in the substrate metabolism, insulin sensitivity, or body composition of obese patients (participants received resveratrol). It is noteworthy that both investigations are characterized by a low number of patients and a relatively short duration.

The impact of curcuminoid on obesity and its associated conditions has been investigated in two of the top 20 research papers, as stated in the papers by Mohammadi et al. [56] and Chuengsamarn et al. [57].

The hydrolysis of carbohydrates and fat primarily involves the participation of α-amylase, α-glucosidase, and pancreatic lipase enzymes, as reported by previous research [58]. Zhang et al. conducted a study that presented the phenolic profiles of various lentil cultivars in Canada and their role in antioxidant activity. On the other hand, Rasouli et al. [59] assessed the inhibitory activity of 26 polyphenols against α-amylase and α-glucosidase through molecular docking and virtual screening studies. The findings suggest that a number of compounds, including caffeic acid, curcumin, cyanidin, daidzein, epicatechin, eridyctiol, ferulic acid, hesperetin, naringenin, pinoresinol, quercetin, resveratrol, and syringic acid, exhibit significant inhibitory effects on the α-glucosidase enzyme. Furthermore, it has been found that catechin, hesperetin, kaempferol, silibinin, and pelargonidin exhibit strong inhibitory effects on α-amylase.

The in vitro study conducted by Hwang et al. [60] demonstrated that chlorogenic acid may be useful in the prevention and treatment of anti-inflammatory diseases. Bogdanski et al. [61] found that green tea extract reduces blood pressure, inflammatory biomarkers, and oxidative stress, and improves parameters associated with insulin resistance in obese, hypertensive patients.

Mitochondrial dysfunction causes numerous human disorders. A platform technology based on biodegradable polymers for carrying bioactive molecules to the mitochondrial matrix could be of enormous potential benefit in treating mitochondrial diseases, as described by Marrachea and Dhar in 2012 [62].

The article by Cai et al. [63] shows that oral advanced glycation endproducts promote insulin resistance and diabetes by depleting the antioxidant defenses advanced glycosylation end products (AGE) receptor-1 and sirtuin 1.

The last most-cited paper by Menni et al. [64] in Table 2 analyzed 16S ribosomal RNA gene sequence data from 1632 healthy females from the TwinsUK registry to determine the correlation between gut microbiome composition and weight gain. Results showed that less than half of the variation in long-term weight change was heritable. Gut microbiota diversity exhibited a negative association with long-term weight gain, while demonstrating a positive correlation with fiber intake. Nine bacterial operational taxonomic units were significantly associated with weight gain, including *Ruminococcaceae* and *Lachnospiraceae*, while *Bacteroides* species were associated with an increased risk of weight gain.

3.4. Density map of keyword authors

We conducted an extraction from the authors' keyword terms of 12557 articles oriented specifically to the identification of antioxidants, herbal species, phytochemicals and natural compounds that are frequently mentioned and which are therefore of particular

Table 3
The 20 most-cited original publications specific to the field, sorted in descending order.

Paper	Title	DOI	TC
Chang C-J, 2015, Nature Communications	Ganoderma lucidum reduces obesity in mice by modulating the composition of the gut microbiota	10.1038/ncomms8489	831
Anhê Ff, 2015, Gut	A polyphenol-rich cranberry extract protects from diet-induced obesity, insulin resistance and intestinal inflammation in association with increased *Akkermansia* spp. population in the gut microbiota of mice	10.1136/gutjnl-2014-307142	792
Liu J, 2015, Cell	Treatment of Obesity with Celastrol	10.1016/j.cell.2015.05.011	482
Zhang X, 2012, PLOS One	Structural Changes of Gut Microbiota during Berberine-Mediated Prevention of Obesity and Insulin Resistance in High-Fat Diet-Fed Rats	10.1371/journal.pone.0042529	479
Wu T-R, 2019, Gut	Gut commensal Parabacteroides goldsteinii plays a predominant role in the anti-obesity effects of polysaccharides isolated from Hirsutella sinensis	10.1136/gutjnl-2017-315458	406
Poulsen Mm, 2013, Diabetes	High-Dose Resveratrol Supplementation in Obese Men: An Investigator-Initiated, Randomized, Placebo-Controlled Clinical Trial of Substrate Metabolism, Insulin Sensitivity, and Body Composition	10.2337/db12-0975	377
Marrache S, 2012, Proc PNAS USA	Engineering of blended nanoparticle platform for delivery of mitochondria-acting therapeutics	10.1073/pnas.1210096109	370
Hwang Sj, 2014, Inflamm Res	Anti-inflammatory effects of chlorogenic acid in lipopolysaccharide-stimulated RAW 264.7 cells	10.1007/s00011-013-0674-4	332
Zhang Z, 2014, Nature Communications	Berberine activates thermogenesis in white and brown adipose tissue	10.1038/ncomms6493	313
Porras D, 2017, Free Radic Biol Med	Protective effect of quercetin on high-fat diet-induced non-alcoholic fatty liver disease in mice is mediated by modulating intestinal microbiota imbalance and related gut-liver axis activation	10.1016/j. freeradbiomed.2016.11.037	311
Zhang B, 2015, Food Chem	Phenolic profiles of 20 Canadian lentil cultivars and their contribution to antioxidant activity and inhibitory effects on α-glucosidase and pancreatic lipase	10.1016/j. foodchem.2014.09.144	308
Jeon Bt, 2012, Diabetes	Resveratrol Attenuates Obesity-Associated Peripheral and Central Inflammation and Improves Memory Deficit in Mice Fed a High-Fat Diet	10.2337/db11-1498	275
Cai W, 2012, Proc Natl Acad Sci U S A	Oral advanced glycation endproducts (AGEs) promote insulin resistance and diabetes by depleting the antioxidant defenses AGE receptor-1 and sirtuin 1	10.1073/pnas.1205847109	247
Bogdanski P, 2012, Nutr Res	Green tea extract reduces blood pressure, inflammatory biomarkers, and oxidative stress and improves parameters associated with insulin resistance in obese, hypertensive patients	10.1016/j.nutres.2012.05.007	241
Rasouli H, 2017, Food Funct	Differential α-amylase/α-glucosidase inhibitory activities of plant-derived phenolic compounds: a virtual screening perspective for the treatment of obesity and diabetes	10.1039/c7fo00220c	238
Mohammadi A, 2013, Phytother Res	Effects of Supplementation with Curcuminoids on Dyslipidemia in Obese Patients: A Randomized Crossover Trial	10.1002/ptr.4715	232
Faghihzadeh F, 2014, Nutr Res	Resveratrol supplementation improves inflammatory biomarkers in patients with nonalcoholic fatty liver disease	10.1016/j.nutres.2014.09.005	231
Chachay Vs, 2014, Clin Gastroenterol Hepatol	Resveratrol Does Not Benefit Patients with Nonalcoholic Fatty Liver Disease	10.1016/j.cgh.2014.02.024	225
Chuengsamarn S, 2014, J Nutr Biochem	Reduction of atherogenic risk in patients with type 2 diabetes by curcuminoid extract: a randomized controlled trial	10.1016/j.jnutbio.2013.09.013	223
Menni C, 2017, Int J Obes	Gut microbiome diversity and high-fibre intake are related to lower long-term weight gain.	10.1038/ijo.2017.66	221

TC = Total citations. All numbers are derived from Scopus on April 17, 2023.

interest for further study. In order to reduce the likelihood of producing inaccurate results, the search terms that were included in the query were removed. The result is displayed through the utilization of a density map (Fig. 8). The density map depicted the frequency of the author's keywords, where the chromaticity associated with the keywords is positively correlated with their frequency, with blue denoting a lower frequency and yellow indicating a higher frequency. The keywords in the central part constitute a core with a greater degree of occurrence.

In Table 4, the author keywords that have a frequency of occurrence greater than 10 are listed. Some terms have been merged into one entry (i.e., tea, green tea and black tea with *Camelia sinensis*, turmeric with *Curcuma longa,* and acid ascorbic with vitamin C). Furthermore, for each term, one bibliographic reference relative to efficacy is provided.

The data revealed that certain herbal species have a higher frequency of occurrence than others. In particular, we found that the top 10 herbs in order of occurrence are *Camelia sinensis*, *Momordica charantia*, *Curcuma longa*, *Ilex paraguariensis*, *Panax ginseng*, *Moringa oleifera*, *Garcinia cambogia*, *Garcinia mangostana*, *Zingiber officinale* and *Cinnamomum verum*. In the group of antioxidants, phytochemicals, and natural compounds, the top 10 were resveratrol, curcumin, quercetin, vitamin E, alpha-lipoic acid, vitamin C, chlorogenic acid, lycopene, fucoxanthin, and berberine.

3.5. Analysis of trend topics: co-occurrence in author's keywords

To identify the most relevant themes and predict probable future trends, a co-occurrence analysis of author's keywords from 12557 articles obtained from the Scopus database was performed. Excluded from consideration were items that lacked any discernible

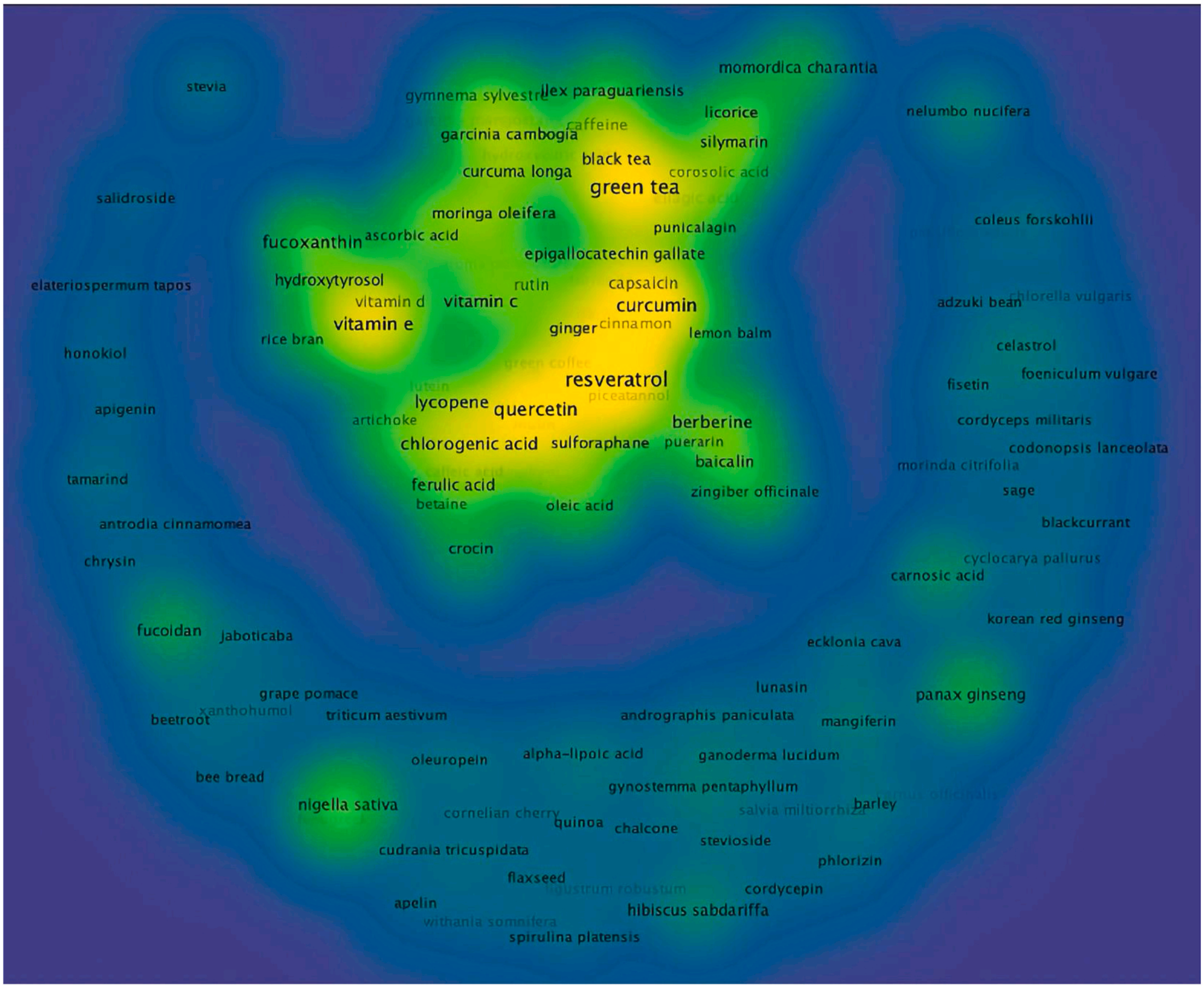

Fig. 8. The density map of the authors' keyword terms refers exclusively to antioxidants, herbal species, phytochemicals and natural compounds. The chromaticity associated with the keywords is positively correlated with their frequency, with blue denoting lower frequency and yellow indicating higher frequency. All numbers are derived from Scopus on April 17, 2023. This network was generated by VOSviewer.

connection to the others. The map depicted in Fig. 9 displays a node that has been assigned a keyword, and the edge connecting the two nodes signifies the co-occurrence of said keywords. The magnitude of the node represents the frequency of the keyword. The degree of co-occurrence between pairs of keywords is indicated by the thickness of the line connecting them, as well as the proximity of the two nodes. The color of the nodes corresponds to the keyword clusters, which often comprise words that appear together and can be construed as overarching research themes within the discipline. The dimensions of the frames portrayed in Fig. 9 are indicative of the frequency of terms found within the author's keywords. The assemblage of interconnected terminologies that constitutes the most extensive collection comprises a total of 649 terms, which have been systematically arranged into four distinct clusters.

The green cluster's core subjects are concerned with the impact of oxidative stress and inflammation on obesity and NAFLD and their role in the progressive evolution of these diseases.

The red cluster's major subjects could be related to factors that lead to metabolic syndrome, obesity and NAFLD comorbidities, such as nutrition, diet, and lifestyle.

The major subjects of the blue cluster could be related to the interest in the relationship between gut microbiota and beneficial properties on obesity and NAFLD, also through pancreatic lipase regulation, of herbal species, antioxidants, phytochemicals and natural compounds.

The yellow cluster is correlated with the research on anti-adipogenesis targets through in vitro (hegp2 cells, 3t3-l1 cells) and in vivo models (high-fat diet animals) of obesity/NAFLD. Among the keywords related to the most frequent targets, we found AMPK (5′ adenosine monophosphate-activated protein kinase) and SIRT-1 (Sirtuin 1).

Table 4
Antioxidants, herbal species, phytochemicals and natural compounds (ranked in order of frequency) that have demonstrated beneficial activity for obesity and NAFLD.

Rank	Herbal species	Obesity Ref.	NAFLD Ref.	Rank	Antioxidants/Phytochemicals/Natural compounds	Obesity Ref	NAFLD Ref.
1	*Camelia sinensis (tea)*	[65]	[66]	1	Resveratrol	[67]	[68]
2	*Momordica charantia (bitter melon)*	[69]	[70]	2	Curcumin	[71]	[72]
3	*Curcuma longa*	[73]	[74]	3	Quercetin	[75]	[76]
4	*Ilex paraguariensis (yerba mate)*	[77]	[78]	4	Vitamin E	[79]	[80]
5	*Panax ginseng (red ginseng)*	[81]	[82]	5	Alpha-Lipoic Acid	[83]	[84]
6	*Moringa oleifera*	[85]	[86]	6	Vitamin C	[87]	[88]
7	*Garcinia cambogia*	[89]	[90]	7	Chlorogenic Acid	[91]	[92]
8	*Garcinia mangostana*	[93]	[94]	8	Lycopene	[95]	[96]
9	*Zingiber officinale (ginger)*	[97]	[98]	9	Fucoxanthin	[99]	[100]
10	*Cinnamomum verum (cinnamon)*	[101]	[102]	10	Berberine	[103]	[104]
11	*Nigella sativa*	[105]	[106]	11	Silymarin	[107]	[108]
12	*Allium sativum (garlic)*	[109]	[110]	12	Astaxanthin	[111]	[112]
13	*Kaempferia parviflora (black ginger)*	[113]	[114]	13	Rutin	[115]	[116]
14	*Glycyrrhiza glabra (licorice)*	[117]	[118]	14	Caffeine	[119]	[120]
15	*Gymnema sylvestre*	[121]	[122]	15	Ellagic Acid	[123]	[124]
16	*Hibiscus sabdariffa*	[125]	[126]	16	Vitamin D	[127]	[128]
17	*Morus alba (mulberry leaf)*	[129]	[130]	17	Capsaicin	[131]	[132]
18	*Aloe vera*	[133]	[134]	18	Epigallocatechin Gallate	[135]	[135]
19	*Coffea arabica/robusta (green coffee)*	[136]	[137]	19	Gallic Acid	[138]	[139]
20	*Gynostemma pentaphyllum*	[140]	[141]	20	Hydroxytyrosol	[142]	[143]
21	*Crocus sativus (saffron)*	[144]	[145]	21	Luteolin	[146]	[147]
22	*Gardeniae fructus*	[148]	[149]	22	Sulforaphane	[150]	[151]
-	-	–	–	23	Crocin	[152]	[153]
-	-	–	–	24	Fucoidan	[154]	[155]
-	-	–	–	25	Baicalein	[156]	[157]
-	-	–	–	26	Ferulic Acid	[158]	[159]
-	-	–	–	27	Chitosan	[160]	[161]
-	-	–	–	28	Thymoquinone	[162]	[163]
-	-	–	–	29	Celastrol	[164]	[165]
-	-	–	–	30	Genistein	[166]	[167]
-	-	–	–	31	Oleanolic Acid	[168]	[169]
-	-	–	–	32	Hesperidin	[170]	[171]
-	-	–	–	33	Oleuropein	[172]	[173]

4. Discussion

Multiple scientific studies have provided evidence of a positive relationship between the intake of phytochemicals, herbs, and other naturally occurring compounds, and their respective health advantages. These benefits encompass but are not restricted to, the mitigation of cancer [174,175], cardiovascular illnesses [176,177], and ocular disorders [178–180]. The present study involves an analysis of a selected collection of articles to track the progression of knowledge related to the application of antioxidants, herbs, phytochemicals and natural compounds, for the treatment of obesity and non-alcoholic fatty liver disease (NAFLD). We have analyzed data obtained from the Scopus database. The bibliometric analysis study yielded a total of 12557 articles within the searched field, spanning from 2012 to 2022. As illustrated in Fig. 1, there has been a continuous annual growth rate of around 10 % since 2012. When compared to the other journals, we observed that the journal *Nutrients* has the most articles (555). Following closely in second place was the journal *Food and Function* with 248 publications (Fig. 2A). *Nutrients* and *Food and Function* are two highly productive journals that cover a wide range of themes. Dietary disorders, metabolic syndrome, nutritional supplements, molecular microbiology, molecular metabolism, molecular pathology, diagnostics and therapeutics, bioactive, nutraceuticals, food, its (micro) constituents, and their correlation with health and/or nutrition are all examples of these types of topics. Research into the application of antioxidants, herbs, phytochemicals and natural compounds for the control of obesity and NAFLD is in line with the focus of the aforementioned journals. The triad of the three journals that have the highest productivity is also the one with the highest citations (Fig. 2B). In fact, *Nutrients*, *PLOS One*, and *Food and Function* dominate the ranking. Upon conducting a detailed analysis of the publication trend per year (as presented in Table 1) of the top 20 most prolific journals, it has been observed that certain journals have exhibited a heightened level of interest in the field over the past decade. Notably, there is a discernible rise in the number of articles published in six journals between 2021 and 2022. The *Journal of Nutritional Biochemistry* exhibits the highest increase, followed by *Nutrients* and *Antioxidants*. Furthermore, it is noteworthy that a total of three out of the top 20 most prolific journals have not experienced any growth in publication output. Conversely, the remaining 11 journals have exhibited a yearly decline in the number of articles published since 2021. The bibliographic coupling of journals (Fig. 3) illustrates the relationship between journals based on the number of shared references and reveals the existence of four clusters. Each cluster represented a collection of journals that demonstrated a citation pattern that was

Fig. 9. Clustered co-occurrence map of the author's keywords from 12557 Scopus-retrieved articles. Only keywords with ten or more occurrences were examined. Items that are unrelated to others were left out. The size of the frames in the map represents how frequently the keyword appears. The proximity of two nodes and the thickness of the line connecting them show the strength of co-occurrence between pairs of keywords. The color of the frames represents keyword clusters, which are typically made up of co-occurring phrases and can be thought of as large research topics in the field. The largest collection of related terms consists of 649 terms divided into four categories, each distinguished by a different color: red, green, yellow, and blue. All numbers are derived from Scopus on April 17, 2023. This network was generated by VOSviewer.

similar to the others. According to Fig. 4A, China, Korea, and the USA have emerged as prominent contributors in the field, based on the number of publications. However, as previously stated, Spain displays the highest Multi Country Publications (MCP) ratio. Meanwhile, it is noteworthy that countries such as Spain and Italy demonstrate a relatively higher incidence of Single Country Publications (SCP) in comparison to MCP. Based on the data presented in Fig. 4B, it can be inferred that China is the leading country in this specific field of study for the number of citations, with the United States and Korea in close pursuit. The large amount of their research published in peer-reviewed journals gives these nations significant influence. Spain, Japan, India, and Italy are observed to have a significant average citation rate, which implies that they have received a noteworthy number of citations in proportion to their published articles. The analysis of cooperative activities among nations, as illustrated in Fig. 5, has revealed the existence of numerous groupings of collaborations. China has formed significant collaborative relationships with several countries, including Australia, Malaysia, Saudi Arabia, Iran, and Korea. Furthermore, Korea has forged direct collaborative partnerships with Hong Kong, Indonesia, Iraq, and Thailand. The United States established a robust partnership with Japan and Sweden, while simultaneously establishing a system of alliances with China. The red and violet clusters are primarily composed of Eurozone countries, although they also encompass the United Kingdom, Brazil, Argentina, and Chile.

The indicator of national output in this field has a strong correlation with the number of institutions involved in scientific production (Table 2 and Fig. 5). The development of Shanghai University of Traditional Chinese Medicine and Kyung Hee University is especially notable when compared to other top universities started in 2019 (Fig. 6), as shown by an analysis of the trend articles produced by the top 10 most prolific institutions.

The evaluation of citations is a significant measure for assessing the influence of an academic publication within a specific discipline. The top 20 original papers that received the most citations from the field's pertinent literature were then displayed in Table 3.

Fig. 8 paints a picture of the most promising antioxidants, herbal species, phytochemicals and natural compounds for the treatment of obesity and NAFLD. The results of our analysis indicate that the ten most commonly found herbs, as shown in Table 4, are *Camelia sinensis, Momordica charantia, Curcuma longa, Ilex paraguariensis, Panax ginseng, Moringa oleifera, Garcinia cambogia, Garcinia* *mangostana, Zingiber officinale, and Cinnamomum verum*. These herbs are listed in descending order of frequency. While the top ten antioxidants, natural compounds, and phytochemicals are resveratrol, curcumin, quercetin, vitamin E, alpha-lipoic acid, vitamin C, chlorogenic acid, lycopene, fucoxanthin, and berberine.

One intriguing aspect of bibliometric analysis concerns the examination of emerging topics. Through the application of co-occurrence keyword analysis, it becomes feasible to produce visual depictions of interesting themes and forecast potential forthcoming trends.

As seen before in Fig. 9, the co-occurrence analysis revealed four topics pertaining to antioxidants, herbs, and natural compounds in the context of obesity and NAFLD (Fig. 9). In addition to the impact of oxidative stress and inflammation on obesity and NAFLD and their involvement in the advancement of these conditions (green cluster), there is an emerging area of research (blue cluster) that centers on the beneficial effects of antioxidants, herbs, and natural compounds on obesity and NAFLD through the modulating the gut microbiota.

The human gastrointestinal tract contains a wide variety of microbial species that play a crucial role in regulating various biological processes. Obesity and chronic liver diseases are just two examples of metabolic disorders that have been linked to dysbiosis in the gut microbiome [181,182]. Increases in BMI are associated with an elevated risk of developing NAFLD [183]. Obesity-related dysbiosis promotes NAFLD progression [184]. Dietary patterns and nutrient consumption are strongly correlated with the diversity, composition, and metabolic activity of the gut microbiome [185,186]. Furthermore, dietary interventions have the potential to modify the composition and functioning of the gastrointestinal microbiome. This, in turn, could potentially contribute to the improvement of coexisting conditions like metabolic syndrome and NAFLD, as well as slow down their advancement into more severe manifestations [187,188]. Antioxidants found in food are essential nutrients that are required by the human body to counteract the oxidative stress that arises from a variety of biochemical and metabolic reactions [189]. The symbiotic relationship between the gut microbiota and antioxidants is crucial for the preservation of homeostasis in the gut microbiome [190]. This connection makes it easier for bacteria to grow In the gut and changes the way antioxidants work by Increasing the production of bioactive metabolites through the microbiome [191]. The ingestion of dietary phytochemicals has the potential to interact with the gut microbiota in a bidirectional manner, resulting in the selective promotion or inhibition of microbial growth and proliferation [192–194]. In fact, a significant correlation was observed between specific classes of phytochemicals and changes in the responding gut microbiota [46,56,57,194,195].

According to several studies, flavonoids are capable of preserving the equilibrium of the gut microbiota by inhibiting the proliferation of detrimental bacteria while promoting the growth of advantageous microorganisms [196]. Tea (*Camelia sinensis*) is comprised of a variety of polyphenols, polysaccharides, and tea saponins. The modulation of gut microbiota by tea has been the subject of research, with findings indicating its potential beneficial effects [197,198]. The consumption of tea has demonstrated a prebiotic-like impact and has the potential to ameliorate gut-microbiota dysbiosis induced by various disease models [197,198]. Curcumin is a bioactive constituent that is found in *Curcuma longa*. The findings of a colonic simulation study conducted in vitro indicate that curcumin is capable of stimulating the production of butyric and propionic acids. The metabolic and biotransformation processes of curcumin can lead to the production of various phenolic compounds [199]. Resveratrol is a naturally occurring phytoalexin that is present in red wine. The administration of resveratrol resulted in an increase in the abundance of advantageous microorganisms, specifically *Lactobacillus* and *Bifidobacterium* spp., and a notable enhancement in the metabolism of bile acids [200]. As aforementioned, berberine has demonstrated effectiveness in preventing the development of insulin resistance and obesity in rats that were administered a high-fat diet. It is hypothesized that this phenomenon is attributable, to some extent, to the alteration of the gut microbiota's structure, which could potentially mitigate inflammation by reducing the host's exogenous antigen burden and elevating the concentration of short-chain fatty acids in the intestinal tract [48]. The potential of *Momordica charantia* to improve insulin sensitivity in obese rats is attributed, at least in part, to its ability to alleviate inflammation in both the systemic environment and white adipose tissues [194,201]. Furthermore, this beneficial effect is linked to the proportional modulation of specific gut microbiota [194,201]. The ingestion of *Ilex paraguariensis* has been linked to various health benefits, including its antioxidant properties, ability to protect the heart, reduce inflammation, and combat obesity [78,202]. Phenolic compounds are the primary constituents found in *Ilex paraguariensis* and have been documented to exhibit a regulatory effect on the microbiome [78,202].

One proposed approach to addressing the issue of obesity and NAFLD, involves the implementation of a specific strategy aimed at diminishing the process of lipid digestion and absorption into the systemic circulation. This can be achieved through the inhibition of phospholipase activity [203]. The utilization of plant-derived natural compounds exhibiting anti-lipase activity has garnered significant interest in the field of healthcare product development due to their advantageous characteristics such as low toxicity and structural variability [204]. In addition, it has been observed that natural products demonstrate efficacy in mitigating the risk of pancreatitis [205]. Pancreatitis is a prominent complication associated with gastrointestinal disorders, frequently triggering and intensifying systemic inflammatory reactions [206]. The gut microbiota is believed to play a crucial role in the regulation of proinflammatory cytokines, which have a significant impact on the progression of pancreatitis [207]. Therefore, the regulation of gut microbiota through the use of antioxidants, herbs, phytochemicals, and natural products may serve as a potential strategy for regulating pancreatic growth, exocrine function, and associated pathologies [208].

The prevalence of metabolic syndrome is influenced by the nutritional imbalance resulting from sedentary lifestyles and excessive food intake. This topic theme emerges in the red cluster. The current state of research indicates that both obesity and insulin resistance are influential factors in the development of NAFLD [12]. When considering the factors that contribute to the accumulation of excessive calories resulting in obesity, it is reasonable to explore an imbalance in energy homeostasis as the fundamental cause [209].

Another theme is the research on anti-adipogenesis molecular targets through in vitro (hegp2 cells, 3t3-l1 cells) and in vivo models (high-fat diet animals) of obesity/NAFLD (cluster yellow). De novo lipogenesis is widely recognized as a crucial element in the pathogenesis of NAFLD [210,211]. Consequently, the inhibition of de novo lipogenesis holds significant promise as a therapeutic target for the prevention of this hepatic disorder. There exists evidence suggesting that AMPK (5′ adenosine monophosphate-activated protein kinase) and SIRT-1 (Sirtuin 1) potentially possess significant importance in de novo lipogenesis and serve as regulatory proteins in the context of type 2 diabetes mellitus, and obesity [212]. Hence, it is plausible to consider AMPK and SIRT1 as potential therapeutic targets for the management of NAFLD. Several natural compounds have been shown to interact with the above molecular targets. For example, flavonoid resveratrol has been found to effectively restore the levels of nicotinamide adenine dinucleotide+ (NAD+), a coenzyme that plays a crucial role in redox reactions [213]. This restoration is achieved through the inhibition of poly (ADP-ribose) polymerase and the activation of the SIRT1/AMPK pathway, both in vitro and in vivo [213]. There is a correlation between reduced AMPK activity and the occurrence of de novo lipogenesis in NAFLD [214]. Therefore, silybin's possible association with a decrease in de novo lipogenesis suggests that AMPK activation is beneficial. Resveratrol is recognized as a powerful activator of AMPK [215]. It has been observed that resveratrol enhances the phosphorylation of AMPK and inhibits the liver X receptor, leading to a decrease in Sterol Regulatory Element-Binding Protein 1C, which is responsible for the processes of lipogenesis and lipid accumulation [216]. In addition, it has been observed that resveratrol, a well-established activator of SIRT 1, exerts inhibitory effects on liver inflammation mediated by autophagy [217]. AMPK and SIRT1 are linked to the mTOR (mechanistic target of rapamycin) and PI3K/Akt (Phosphoinositide 3-kinase/Akt serine-threonine kinase) pathways through processes of phosphorylation, inhibition, and deacetylation, which control cellular balance and physiological functions [218–220]. Multiple studies have demonstrated that antioxidants can regulate the mTOR and PI3K/Akt pathways in order to preserve redox equilibrium [218,221]. The mTOR pathway stimulates the activation of antioxidant defense mechanisms [222]. Moreover, the PI3K/Akt pathway activates antioxidant genes and is modulated by oxidative stress [218,223,224]. The PI3K/Akt and mTOR pathways are linked, with mTOR exerting influence on PI3K/Akt activity and vice versa [218,223,224]. As a result, antioxidants, such as resveratrol, are able to regulate this interaction by preserving a steady state of redox equilibrium. Moreover, according to Huang et al. [225], the administration of resveratrol demonstrated enhancements in lipid metabolism, redox homeostasis, and oxidative stress in rats with NAFLD induced by a high-fat diet. These improvements were attributed to the activation of the protein kinase A/AMPK/peroxisome proliferator-activated receptors (PPARs) signaling pathway [225].

5. Conclusions

The analysis presented in this study offers valuable insights for researchers investigating the efficacy of antioxidants, herbs, phytochemicals and natural compounds in addressing obesity and non-alcoholic fatty liver disease (NAFLD). By employing bibliometric methods, the study provides a comprehensive and enlightening overview. Moreover, the findings of this analysis can serve as a basis for future research endeavors in this particular domain. It is apparent that bibliometric analysis serves as a valuable tool for extracting valuable knowledge and identifying patterns. Nevertheless, it is important to acknowledge that a potential limitation of the present study lies in the fact that our publications exclusively derive from the Scopus database.

Ethics declarations

Review and/or approval by an ethics committee was not needed for this study because this article does not contain any studies with human participants or animals. Informed consent was not required for this study because this article does not contain any studies with human participants.

Consent to publication

Not applicable.

Data availability statement

The original contributions presented in this study are included in the article and its supplementary materials. No data were deposited in any publicly available repositories. Further inquiries can be directed to the corresponding authors.

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Salvatore Pezzino: Writing – review & editing, Writing – original draft, Visualization, Software, Formal analysis, Data curation, Conceptualization. **Maria Sofia:** Writing – review & editing, Visualization. **Chiara Mazzone:** Writing – review & editing, Visualization. **Giorgia Litrico:** Writing – review & editing, Visualization. **Luigi Piero Greco:** Writing – review & editing, Visualization. **Luisa Gallo:** Writing – review & editing, Visualization. **Gaetano La Greca:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis. **Saverio Latteri:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Resources, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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