Bibliometric Analysis of *Sargassum* Potential in Diabetes Mellitus Management

Agung Giri Samudra [1,2], *Agung* Endro Nugroho[3*], and *Retno* Murwanti[3,4]

[1] Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta 55281, Indonesia
[2] Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Bengkulu University. Bengkulu 38371, Indonesia
[3] Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta 55281, Indonesia
[4] Medicinal Plants and Natural Products Research Center, Faculty of Pharmacy, Universitas Gadjah Mada, 55281 Yogyakarta, Indonesia

Abstract. The prevalence of diabetes mellitus (DM) has increased significantly, with *Sargassum* emerging as a potential therapeutic agent. Despite the abundant literature on *Sargassum* antidiabetic properties, bibliometric analyses have yet to be conducted. This study aimed to bridge this gap by conducting a bibliometric analysis of existing articles on preclinical trials of *Sargassum* for managing DM. Leveraging Scopus, we compiled a bibliographic database encompassing primary research articles in this domain. Sixty-four publications spanning from 2008 to 2023 were meticulously selected for analysis. These articles underwent bibliometric scrutiny using the RStudio® and VOS viewer applications. China emerged as the most influential country, with the South China University of Technology leading among institutions and the International Journal of Biological Macromolecules serving as the primary source. Notably, Chao Li was identified as the most impactful author in this domain. The study covered phytochemistry and pharmacology, which were the predominant and diverse fields. Our findings encourage research collaboration and illuminate critical research gaps essential for advancing the applications of herbal medicine.

1 Introduction

Diabetes mellitus (DM) is a metabolic illness marked by high blood sugar levels due to insufficient insulin synthesis or impaired effectiveness. Insulin regulates blood sugar levels by facilitating glucose uptake from the blood and storing it for energy or later use. Deficiencies in insulin production can result in either low or high blood sugar levels, contributing to severe health issues such as heart disease, tissue damage, stroke, kidney failure, blindness, and potentially fatal outcomes if not addressed [1]. According to the International Diabetes Federation Diabetes Atlas, projections indicate that by 2030, approximately 643 million people aged 20-79 will live with diabetes, representing a prevalence of 11.3%. This figure is expected to rise to 783 million by 2045, with a prevalence of 12.2% [2]. In addition to its widespread occurrence, diabetes mellitus poses a health challenge, diminishing the overall quality of life, leading to fatalities, and impacting economic expenditures [3]. Natural products are a viable approach for preventing and treating the condition [4].

Recently, there has been a notable increase in the utilization of various medicinal plants for treating diabetes mellitus (DM). Among these, the antidiabetic properties of *Sargassum* extract have attracted attention, especially in studies involving mice with type 2 diabetes mellitus (T2DM). This extract has demonstrated efficacy in reducing multiple symptoms associated with T2DM, including oxidative stress, insulin resistance, hyperglycemia, hyperlipidemia, and liver and pancreatic tissue damage [5]. Additionally, *Sargassum wightii*, a species known for its medicinal potential, contains fucoidan, a naturally occurring polysaccharide renowned for its various biological functions. Fucoidan has been documented to exhibit antidiabetic, antioxidant, and anti-inflammatory properties, emphasizing its significant therapeutic potential [6]. Furthermore, research on *Sargassum wightii* has led to the isolation, which has shown promise in inhibiting α-amylase and α-glucosidase enzymes. This inhibition reduces postprandial hyperglycemia and potentially lowers the risk of developing diabetes [7]. Moreover, animal models of diabetes have also demonstrated that *Sargassum horneri* can regulate blood sugar levels

* Corresponding author: nugroho_ae@ugm.ac.id

effectively. *Sargassum horneri* can serve as a valuable functional additive in diabetes treatment and as a healthy food option, emphasizing its dual role in addressing health concerns and environmental sustainability [8]. While numerous scientific publications explore the antidiabetic potential of *Sargassum* sp., primarily through original research and reviews, a bibliometric analysis of this field is yet to be conducted. To address this gap and advance research in this area, this study employs a bibliometric approach focusing on *Sargassum* sp. in the context of diabetes mellitus (DM). The bibliometric analysis encompasses both managerial and theoretical aspects, involving literature evaluations to assess authors, institutions, and sources, informing policymaking, research funding priorities, and fostering collaboration among researchers [9-11]. Furthermore, exploring theoretical aspects through bibliometric studies helps discern publication trends and anticipate future directions in particular fields of study. This study, therefore, proposes a novel quantitative approach to investigating the antidiabetic properties of *Sargassum* sp, aligns with previous research efforts, and offers valuable insights for guiding future investigations.

2 Materials and methods

2.1 Data source

The Scopus database, renowned for its comprehensive collection of scientific papers, was chosen as the data source for this bibliometric analysis due to its extensive coverage [9]. On April 18, 2024, a search was conducted in the Scopus database using the keywords "*Sargassum*" AND diabet* OR "diabetes mellitus" OR dm OR insulin OR glucose. These keywords were applied within scientific journals' titles, abstracts, or keyword sections. Inclusion criteria for articles retrieved from the Scopus database were primary research articles written in English or other indexed languages, focusing on utilizing *Sargassum* sp. as a treatment for diabetes in preclinical investigations. The exclusion criteria were studies conducted on models not exhibiting prediabetic or diabetic conditions (in vitro or in vivo), research focused solely on antioxidant activity without clear relevance to prediabetic or diabetic contexts, and articles lacking sufficient or complete text [12]. The process of data extraction and analysis is illustrated in Figure 1.

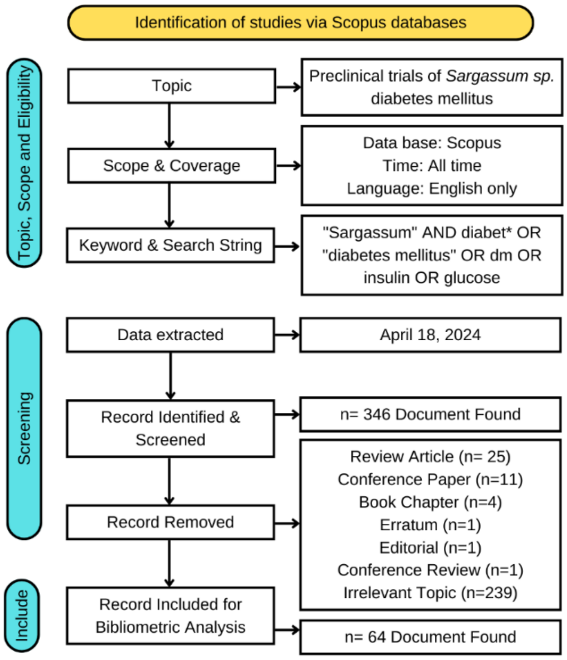


Fig. 1. Search process methodology

2.2 Data extraction and analysis

The relevant documents were saved in the ".CSV" format and then imported into the BiblioShiny program, a software suite compatible with the RStudio® and VOSviewer platforms, facilitating the bibliometric analysis [13] [14]. This software suite streamlined the evaluation process, enabling analysis of publication trends, impactful countries, contributing sources, prominent institutions, authors, bibliographical coupling network, most impactful articles, co-citation network, and keyword co-occurrence network. The bubble map visualization featured in the analysis represents a term or phrase. The size of the bubbles and the distance between them indicate word frequency and co-occurrence frequency, respectively. This approach allowed for a comprehensive examination of the data, providing insights into the relationships and patterns within the literature on the topic [15] [16].

3 Results and discussion

3.1 Analysis of publication trends

A total of 64 articles were included in the analysis, spanning the period from 2008 to 2023. These articles involved 45 unique sources and contributions from 263 authors. The earliest relevant article, published in the Journal of the Federation of European Biochemical Societies (FEBS) in 2008, investigated the effect of *Sargassum* on the development of fat cells through the activation of PPARα/γ in 3T3-L1 [17]. Notably, 2023 witnessed the most significant number of publications, with nine articles published. Figure 2 shows the trends in the number of publications every year. Between 2008 and 2015, research advancements occurred using both in vitro and in vivo models. In vitro, studies focused on cellular mechanisms, including the impact on 3T3-L1 cells, PPARs α and γ, adiponectin, GLUT4, α-glucosidase, α-amylase, DPP-IV activity, and insulin secretion by RIN-m5F β cells. In vivo, research investigated BW, BG, TC, TG, LDL, HDL, adiponectin, PPARs, FFA, G6Pase, insulin response, HbA1c, SGOT, SGPT, AST, ALT, ALP, as well as degenerated and necrotic cells in the liver, pancreas, and kidney. Building upon previous advancements between 2008 and 2015, in vitro studies will delve into the molecular mechanisms underlying PPARα and PPARγ activation, including their influence on adiponectin secretion, glucose metabolism pathways (such as GLUT4 expression, α-glucosidase, and α-amylase activity), and insulin secretion. Meanwhile, in vivo investigations will extend these findings to examine systemic effects on body weight regulation, lipid metabolism (TC, TG, LDL, and HDL levels), and glucose homeostasis. In vitro and in vivo studies were conducted from 2016 to 2023 to elucidate the intricate mechanisms underlying diabetes pathogenesis and progression. In vitro, experiments investigated key enzymes (α-amylase, α-glucosidase, DPP-IV) and cellular processes (glucose uptake by HepG2 cells, PTP1B activity) involved in glucose metabolism and insulin signaling. Concurrently, in vivo research investigated BW, BG, TC, LDL, VLDL, HDL, TG, HBA1c, SGOT, SGPT, UA, Cr, FI, WI, BUN, insulin, HOMA-IR, HOMA B, hs-CRP, QUICKI, AI, AST, ALT, IRS-1, PI3K, JNK, SOD, GSH-Px, MDA, bacteroidetes, firmicutes, NF-κB, IL-6, GSK-3β, SREBPs, TNF-α, NQO1, PEPCK, ACC1 and PKB, or Akt. Spanning the years 2016 to 2023, this study builds upon previous research endeavors to elucidate the intricate mechanisms underlying diabetes pathogenesis and progression. In vitro investigations focused on key enzymes and cellular processes involved in glucose metabolism and insulin signaling. These experiments aim to unravel the molecular mechanisms governing glucose homeostasis and insulin sensitivity at the cellular level. Simultaneously, in vivo research explored myriad metabolic, inflammatory, and biochemical parameters associated with diabetes. By integrating findings from both in vitro and in vivo studies, this research provides a comprehensive understanding of the complex molecular and physiological mechanisms contributing to diabetes mellitus. This study employed in vivo models induced by alloxan, STZ, or STZ-nicotinamide and a high-fat diet (HFD) to explore various mechanisms with potential antidiabetic effects. These included enhanced uptake of free fatty acids and glucose by adipocytes, improved insulin sensitivity, inhibition of DPP-IV and sterol regulatory element-binding protein (SREBP) pathways, accelerated healing of diabetic ulcers, and modulation of proteins involved in diabetes development. In vitro studies using cell lines (e.g., IR-HepG2 and 3T3-L1) and non-cellular assays (e.g., DPP-IV assay) investigated the mechanisms identified in vivo.

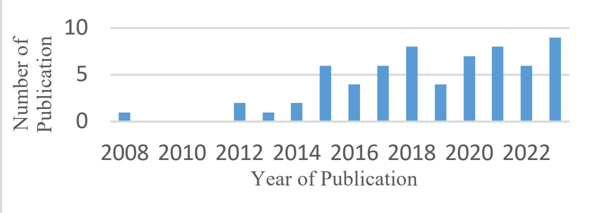
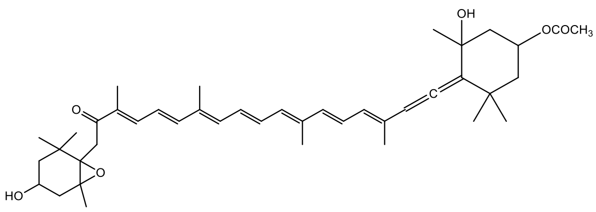
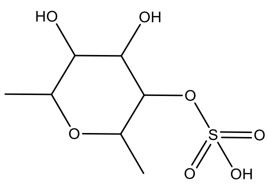


Fig. 2. Trends in *Sargassum* publication in diabetes preclinical studies

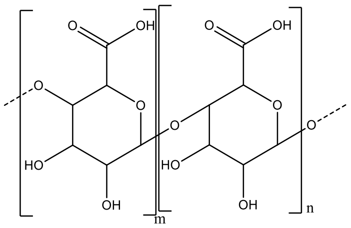
Phytochemical analysis plays a vital role in understanding the chemical composition of traditional medicine, allowing for the identification of potential therapeutic compounds. Pharmacological studies then evaluate the effectiveness, potency, mechanism of action, and target of these compounds, paving the way for new drug development. These investigations utilize both in vitro and in vivo methods. In the field of herbal medicine, researchers test various fractions, including extracts and isolates, either alone or in combination, to elucidate their potential health benefits [18]. Marine macroalgae have emerged as a rich source of promising phytochemicals with antidiabetic potential. Examples include fucoxanthin, fucosterol, fucoidan, alginate, sargahydroquinoic acid, and sargaquinoic acid. The specific *Sargassum* phytochemicals with antidiabetic properties are detailed in Figure 3.



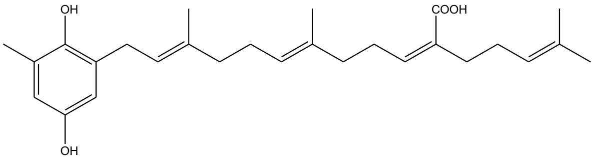
Fucoxanthin [19]



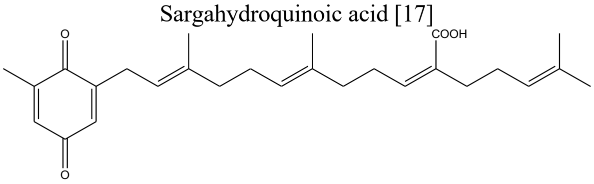
Fucoidan [6]



Alginate [20]



Sargahydroquinoic acid [17]



Sargaquinoic acid [17]

Fig. 3. *Sargassum* phytochemicals with anti-diabetic properties

3.2 Analysis of Impactful Countries

Sixty-four articles from twelve countries (China, Korea, India, Iran, Indonesia, Egypt, Japan, Malaysia, Denmark, Philippines, Portugal, and the USA) investigated the antidiabetic effects of *Sargassum* through preclinical studies. Asia emerged as the most productive region, with China leading in both the number of publications and citations per publication (Table 2 —Most Impactful Countries).

3.3 Analysis of contributing sources

Analysis of publication sources for preclinical studies on *Sargassum*'s antidiabetic properties can inform scholars' publishing choices. Among 45 sources identified, only eight published two or more articles. The International Journal of Biological Macromolecules emerged as the most productive source, publishing nine articles (Table 2- Most Productive Sources).

Table 1. Journal publication document data selected for bibliometric analysis

No	Author	Title	Year	Source	Total Citations	Mechanisms	Reference
1	Xing Xie, Chun Chen, Xiong Fu	Modulation Effects of *Sargassum pallidum* Extract on Hyperglycemia and Hyperlipidemia in Type 2 Diabetic Mice.	2023	Foods	0	The extract could regulate the metabolism of glycolipids in mice with T2DM and alleviate intestinal dysbiosis.	[5]
2	Shanavas Syed Mohamed Puhari, Subramani Yuvaraj, Varadaraj Vasudevan, Tharmarajan Ramprasath, Kulanthaiyesu Arunkumar, Chinnaiah Amutha & Govindan Sadasivam Selvam	Fucoidan from *Sargassum wightii* Reduces Oxidative Stress Through Upregulating Nrf2/HO-1 Signaling Pathway in Alloxan-induced Diabetic Cardiomyopathy rats	2023	Molecular Biology Reports	2	Utilizing fucoidan to combat oxidative stress has proven to be a helpful strategy in preventing diabetic cardiomyopathy.	[6]
3	Young-Hyeon Lee, Hye-Ran Kim, Min-Ho Yeo,Sung-Chun Kim, Ho-Bong Hyun, Young-Min Ham, Yong-Hwan Jung, Hye-Sook Kim, Kyung-Soo Chang	Anti-Diabetic Potential of *Sargassum horneri* and *Ulva australis* Extracts In Vitro and In Vivo.	2023	Current Issues in Molecular Biology	0	Managing blood glucose alleviates α-glucosidase activity inhibition, oxidative stress reduction, insulin resistance, and improvement in oral glucose tolerance.	[8]
4	Vijayan Raji, Chitra Loganathan, Thiyagarajan Ramesh, Palvannan Thayumanavan	Dual Antidiabetic and Antihypertensive Activity of Fucoxanthin Isolated from *Sargassum wightii* Greville in In Vivo Rat Model	2023	Food Science and Human Wellness	1	Reducing high blood sugar levels, reducing damage caused by free radicals, and safeguarding the structure of tissues.	[19]
5	Narasimha Kumar Godlaveti Vijay, Chitra Vellapandian	Ameliorative Effects of Phlorotannin-rich Fraction of *Sargassum tenerrimum* in High-fat Diet and Low Dose Streptozotocin-Induced Metabolic Changes and Oxidative Stress in Diabetic Rats	2023	Journal of Herbmed Pharmacology	1	Antioxidant scavenging activity, effective binding of insulin to its receptors, increase glucose uptake.	[21]
6	Agung Giri Samudra, Nurfijrin Ramadhani, Reza Pertiwi, Dyah Fitriani, Fathnur Sani K, Asril Burhan	Antihyperglycemic activity of nanoemulsion of brown algae (*Sargassum* sp.). Ethanol extract in glucose tolerance test in male mice	2023	Annales Pharmaceutiques Françaises	3	Nanoemulsions derived from *Sargassum* sp. extract have demonstrated the ability to lower blood glucose levels in mice.	[22]
7	Saly Gheda, Ragaa A Hamouda, Mai Abdel Naby, Tarek M. Mohamed, Turki M Al-Shaikh, Abeer Khamis	Potent Effect of Phlorotannins Derived from *Sargassum linifolium* as Antioxidant and Antidiabetic in a Streptozotocin-Induced Diabetic Rats Model	2023	Applied Sciences	4	Phlorotannins, in particular, have potential therapeutic properties such as antioxidant, antidiabetic, anti-cholesterol, and triglyceride-lowering effects.	[23]
8	Niloofar Moheimanian, Hossein Mirkhani, Azar Purkhosrow, Jelveh Sohrabipour, Amir Reza Jassbi	In Vitro and In Vivo Antidiabetic, α-Glucosidase Inhibition and Antibacterial Activities of Three Brown Algae, *Polycladia myrica, Padina antillarum*, and *Sargassum boveanum*, and a Red Alga, *Palisada perforata* from the Persian Gulf	2023	Iranian Journal of Pharmaceutical Research	3	The extracts displayed notable inhibition of α-glucosidase activity, leading to a decrease in glucose levels observed in diabetic rats.	[24]
9	Jeong-Woong Park, Kyung Soo Kang, In Su Ha, Sang In Lee, Sangsu Shin	Efficacy of Fucoxanthin Extract from *Sargassum horneri* on 3T3-L1 Pre-adipocyte Differentiation	2023	Cellular and Molecular Biology	1	The regulation of adipogenesis can be achieved by extracting fucoxanthin from *S. horneri.*	[25]
10	Eldrin DLR. Arguelles	Preliminary Studies on the Potential Antioxidant and Antidiabetic Activities of *Sargassum polycystum* C. Agardh (Phaeophyceae, Ochrophyta)	2022	Jordan Journal of Biological Sciences	2	*S. polycystum* demonstrated strong inhibitory effects on both α-amylase and α-glucosidase enzymes.	[26]

11	Nioofar Moheimanian, Hossein Mirkhani, Jelveh Sohrabipour, Amir Reza Jassbi	Inhibitory Potential of Six Brown Algae from the Persian Gulf on α-Glucosidase and In Vivo Antidiabetic Effect of *Sirophysalis Trinodis*	2022	Iranian Journal of Medical Sciences	10	The extracts exhibited significant α-glucosidase inhibitory activity, leading to a reduction in glucose levels in diabetic rats.	[27]
12	Rui-Bo Jia, Juan Wu, Donghui Luo, Lianzhu Lin, Chong Chen, Chuqiao Xiao, Mouming Zhao	The Beneficial Effects of Two Polysaccharide Fractions from *Sargassum fusiform* against Diabetes Mellitus Accompanied by Dyslipidemia in Rats and Their Underlying Mechanisms	2022	Foods	7	SFP administration could alleviate hyperglycemia, hyperlipemia, organ injury, chronic inflammation, and oxidative stress.	[28]
13	Sovannary Un, Nguyen Van Quan, La Hoang Anh,Vu Quang Lam, Akiyoshi Takami, Tran Dang Khanh, Tran Dang Xuan.	Effects of In Vitro Digestion on Anti-α-Amylase and Cytotoxic Potentials of *Sargassum* spp.	2022	Molecules	10	Inhibition of α-amylase.	[29]
14	Muhamad Firdaus, Rahmi Nurdiani , Bachtiar Rivai, Windy Hapsari Hemassonida, Aqilatul Badzliyah, Nur Khasanah Sugiat	The Glucose Uptake of Type 2 Diabetic Rats by *Sargassum olygocystum* Extract: In Silico and In Vivo Studies	2022	Journal of Applied Pharmaceutical Science	2	The effects of suppressing PTP1B activity and increasing PI3K/Akt expression on lowering rat blood sugar levels.	[30]
15	Mengqing Zhang, Ruijin Yang, Shuhuai Yu, Wei Zhao	A novel α-glucosidase inhibitor polysaccharide from *Sargassum fusiforme*	2022	International Journal of Food Science & Technology	8	SFP-1 had exceptional activity in inhibiting α-glucosidase.	[31]
16	A. Philomena Joy Lindsey, Reya Issac, M. Lakshmi Prabha, R. Emilin Renitta1, Angeline Catherine, Antony V. Samrot, S. Abirami, P. Prakash, S. Dhiva	Evaluation of Antidiabetic Activity of *Sargassum tenerrimum* in Streptozotocin-Induced Diabetic Mice	2021	Journal of Pure and Applied Microbiology	2	Methanolic extract possess anti-diabetic properties.	[32]
17	Mariana Barbosa, Fátima Fernandes, Maria João Carlos, Patrícia Valentão, Paula B. Andrade	Adding Value to Marine Invaders by Exploring the Potential of *Sargassum muticum* (Yendo) Fensholt Phlorotannin Extract on Targets Underlying Metabolic Changes in Diabetes	2021	Algal Research	12	The extract of *S. muticum* demonstrates potential in mitigating oxidative stress and inflammation linked to diabetes through its specific targeting of phlorotannin.	[33]
18	Siya Wu, Jihui Zuo, Yang Cheng, Ya Zhang, Zhongshan Zhang, Mingjiang Wu, Yue Yang	Ethanol Extract of *Sargarsum fusiforme* Alleviates HFD/STZ-induced Hyperglycemia in Association with Modulation of Gut Microbiota and Intestinal Metabolites in Type 2 Diabetic Mice	2021	Food Research International	59	The ethanol extract of *S. fusiforme* effectively reduces the severity of pathological alterations in adipose, liver, and cardiac tissues and the amount of oxidative stress in the liver.	[34]
19	Jian Liu, Siya Wu, Yang Cheng, Qiuhui Liu, Laijin Su, Yue Yang, Xu Zhang, Mingjiang Wu, Jong-il Choi, Haibin Tong	*Sargassum fusiforme* Alginate Relieves Hyperglycemia and Modulates Intestinal Microbiota and Metabolites in Type 2 Diabetic Mice	2021	Nutrients	41	Alginate significantly reduced the levels of BW, FBG, FI, WI consumption and serum lipids in diabetic mice.	[20]
20	Najme Oliyaei, Marzieh Moosavi-Nasab, Ali Mohammad Tamaddon, Nader Tanideh	Antidiabetic effect of fucoxanthin extracted from *Sargassum angustifolium* on streptozotocin-nicotinamide-induced type 2 diabetic mice	2021	Food Science and Nutrition	38	Fucoxanthin demonstrates multifaceted benefits by lowering lipid profile measures, promoting pancreatic beta cell regeneration, and reducing blood glucose levels.	[35]
21	Zhao-Rong Li, Rui-Bo Jia, Juan Wu, Lianzhu Lin, Zhi-Rong Ou, Bingwu Liao, Lixia Zhang, Xun Zhang, Guohui Song, Mouming Zhao	*Sargassum fusiforme* polysaccharide partly replaces acarbose against type 2 diabetes in rats	2021	International Journal of	49	Mitigated diabetic symptoms and improved insulin resistance by	[36]

				Biological Macromolecules		stimulating the IRS/PI3K/AKT signaling pathway.	
22	Shigeru Murakami, Chihiro Hirazawa, Takuma Ohya, Rina Yoshikawa,Toshiki Mizutani, Ning Ma, Mitsuru Moriyama, Takashi Ito, Chiaki Matsuzaki	The Edible Brown Seaweed *Sargassum horneri* (Turner) C. Agardh Ameliorates High-Fat Diet-Induced Obesity, Diabetes, and Hepatic Steatosis in Mice	2021	Nutrients	38	The development of obesity and related metabolic disorders, including diabetes, hepatic steatosis, and hypercholesterolemia.	[37]
23	Young-Hyeon Lee, Min-Ho Yeo, Seon-A Yoon, Ho-Bong Hyun, Young-Min Ham, Yong-Hwan Jung, Kyung-Soo Chang	Effects of *Sargassum horneri* and *Ulva australis* Extracts on Body Weight and Serum Glucose Levels of Sprague-Dawley Rats	2021	Preventive Nutrition and Food Science	4	Weight gain after extract administration was low, and serum biochemistry analyses showed significantly lowered blood sugar levels.	[38]
24	R. Emilin Renitta, Reenu Narayanan, Jane Cypriyana PJ, Antony V. Samrot	Antidiabetic potential of methanolic extracts of *Sargassum wightii* in streptozotocin induced diabetic mice	2020	Biocatalysis and Agricultural Biotechnology	14	*S. wightii* could be used as a potential antidiabetic agent that exhibited significant anti-hyperglycemic activity.	[39]
25	Rui-Bo Jia, Juan Wu, Zhao-Rong Li, Zhi-Rong Ou, Lianzhu Lin, Baoguo Sun, Mouming Zhao	Structural characterization of polysaccharides from three seaweed species and their hypoglycemic and hypolipidemic activities in type 2 diabetic rats	2020	International Journal of Biological Macromolecules	58	SFP prominently could reduce water intake and fasting blood glucose and improve glucose tolerance, hypercholesterolemia, and hypertriglyceridemia in diabetic rats.	[40]
27	Rui-Bo Jia, Zhao-Rong Li, Juan Wu, Zhi-Rong Ou, Qiyuan Zhu, Baoguo Sun, Lianzhu Lin	Physicochemical properties of polysaccharide fractions from *Sargassum fusiforme* and their hypoglycemic and hypolipidemic activities in type 2 diabetic rats	2020	International Journal of Biological Macromolecules	63	SFPs significantly improved hyperglycemia, hyperlipidemia, and liver and kidney function in diabetic rats.	[41]
28	Bin Wei, Qi-Wu Zhong, Song-Ze Ke, Tao-Shun Zhou, Qiao-Li Xu, Si-Jia Wang, Jian-Wei Chen, Hua-Wei Zhang, Wei-Hua Jin, Hong Wang	*Sargassum fusiforme* Polysaccharides Prevent High-Fat Diet-Induced Early Fasting Hypoglycemia and Regulate the Gut Microbiota Composition	2020	Marine Drugs	16	SFPs effectively prevent early fasting hypoglycemia induced by HFD and regulate gut microbiota composition.	[42]
29	Soudeh Bahramian Nasab, Ahmad Homaei, Leila Karami	Kinetic of α-amylase inhibition by *Gracilaria corticata* and *Sargassum angustifolium* extracts and zinc oxide nanoparticles	2020	Biocatalysis and Agricultural Biotechnology	25	*S. angustifolium* algae show inhibitory activity towards α-amylase.	[43]
30	Yao Xian Chin, Xin Chen, Wan Xiu Cao, Yurizam Sharifuddin, Brian D. Green, Phaik Eem Lim, Chang Hu Xue	Characterization of Seaweed Hypoglycemic Property with integration of virtual screening for identification of bioactive compounds	2020	Journal of Functional Foods	16	Extract ameliorated insulin resistance and influenced glucose homeostasis by impacting gluconeogenesis and protecting tissues from HFD-induced damage.	[44]
26	Gehan Ahmed Ismail, Saly Farouk Gheda, Atef Mohamed Abo-Shady, Omnia Hamdy Abdel-Karim	In vitro Potential Activity of some Seaweeds as Antioxidants and Inhibitors of Diabetic Enzymes	2019	Food Science and Technology	89	Extracts exhibited a potent inhibitory activity, in vitro, on α-amylase and α-glucosidase starch hydrolyzing enzymes	[45]
31	Changliang Cao, Chao Li, Qing Chen, Qiang Huang, Manuel Everardo Mondragón Pérez, Xiong Fu	Physicochemical Characterization, Potential Antioxidant and Hypoglycemic Activity of Polysaccharide from *Sargassum pallidum*	2019	International Journal of Biological Macromolecules	48	Inhibitory activities against α- α-glucosidase and amylase, antioxidant and hypoglycemic.	[46]

32	Cheng-feng Yang, Shan-shan Lai, Yi-han Chen, Dan Liu, Bin Liu, Chao Ai, Xu-zhi Wan, Lu-ying Gao, Xin-hua Chen, Chao Zhao	Anti-diabetic Effect of Oligosaccharides from Seaweed *Sargassum Confusum* via JNK-IRS1/PI3K Signalling Pathways and Regulation of Gut Microbiota	2019	Food and Chemical Toxicology	92	Oligosaccharides exhibit hypoglycemic and hypolipidemic effects by regulating hepatic insulin resistance through the IRS1/PI3K and JNK signaling pathways.	[47]
33	Yang Cheng, Luthuli Sibusiso, Lingfeng Hou, Huijing Jiang, Peichao Chen, Xu Zhang, Mingjiang Wu, Haibin Tong	*Sargassum fusiforme* Fucoidan Modifies the Gut Microbiota During Alleviation of Streptozotocin-induced Hyperglycemia in Mice	2019	International Journal of Biological Macromolecules	114	Fucoidan extract improves gastrointestinal health, thereby mediating its beneficial effects on diabetes.	[48]
34	Heng Xiao, Xiong Fu, Changliang Cao, Chao Li, Chun Chen, Qiang Huang	Sulfated Modification, Characterization, Antioxidant and Hypoglycemic Activities of Polysaccharides from *Sargassum pallidum*	2019	International Journal of Biological Macromolecules	117	Polysaccharides extracted from *S. pallidum* exhibit both hypoglycemic and antioxidant effects.	[49]
35	Theodora Linggaryati Gotama, Amir Husni, Ustadi	Antidiabetic Activity of *Sargassum hystrix* Extracts in Streptozotocin-Induced Diabetic Rats	2018	Preventive Nutrition and Food Science	40	The ethanolic extract efficiently lowers both preprandial and postprandial blood glucose levels in diabetic rats without notably affecting their fat profile.	[50]
36	Ji-Soo Lee, Ji-Sook Han	*Sargassum sagamianum* Extract Alleviates Postprandial Hyperglycemia in Diabetic Mice	2018	Preventive Nutrition and Food Science	5	The ethanol extract acts as an inhibitor for both α-glucosidase and α-amylase, effectively retarding the absorption of dietary carbohydrates.	[51]
37	Abdu Rohman Nurfahmi, Amir Husni, Alim Isnansetyo	Effect of *Sargassum hystrix* Powder on the Biochemical Profile of Diabetic Wistar Rats	2018	Pakistan Journal of Nutrition	5	Polyphenols, acting as antioxidants, decrease enzyme activity in carbohydrate breakdown into glucose, whereas alginate polysaccharides inhibit glucose absorption in the intestines.	[52]
38	Nazikussabah Zaharudin, Armando Asunción Salmeán, Lars Ove Dragsted	Inhibitory Effects of Edible Seaweeds, Polyphenolics and Alginates on the Activities of Porcine Pancreatic α-amylase	2018	Food Chemistry	78	gallic acids, 2,5-dihydroxybenzoic acids, and alginates exhibit strong inhibition of α-amylase activity.	[53]
39	Changliang Cao, Qiang Huang, Bin Zhang, Chao Li, Xiong Fu	Physicochemical Characterization and In Vitro Hypoglycemic Activities of Polysaccharides from *Sargassum pallidum* by Microwave-assisted Aqueous Two-phase Extraction	2018	International Journal of Biological Macromolecules	101	The compound demonstrates inhibitory effects on both α-amylase and α-glucosidase enzymes, significantly boosting glucose consumption and fostering the growth of IR-HepG2 cells.	[54]
40	Samad Akbarzadeh, Hossein Gholampour, Parviz Farzadinia, Adel Daneshi, Bahman Ramavandi, Ali Moazzeni, Mojtaba Keshavarz, and Afshar Bargahi	Anti-diabetic Effects of *Sargassum oligocystum* on Streptozotocin-induced Diabetic Rat	2018	Iranian Journal of Basic Medical Sciences	42	The extract improves diabetes by reducing insulin resistance, lowering glucose levels, and regenerating damaged pancreatic β-cells.	[55]
41	Misung Kwon, Su-Jin Lim, Bonggi Lee, Taisun Shin, Hyeung-Rak Kim	Ethanolic Extract of *Sargassum serratifolium* Inhibits Adipogenesis in 3T3-L1 Preadipocytes by Cell Cycle Arrest	2018	Journal of Applied Phycology	16	The extract inhibited adipocyte differentiation early on and lipid accumulation during adipogenesis by downregulating adipogenic and lipogenic transcription factors.	[56]
42	Muhamad Firdaus, Anies Chamidah	*Sargassum Polycystum* Methanol Extract Affects the Nuclear Factor-k Beta and	2018	Asian Journal of Pharmaceutical	2	The methanol extract shows promise as an anti-inflammatory agent in diabetes.	[57]

		Interleukin-6 Expression in Streptozotocin-induced Diabetes Rats.		and Clinical Research			
43	Md. Yousof Ali, Da Hye Kim, Su Hui Seong, Hyeung-Rak Kim, Hyun Ah Jung, Jae Sue Choi	α-Glucosidase and Protein Tyrosine Phosphatase 1B Inhibitory Activity of Plastoquinones from Marine Brown Alga *Sargassum serratifolium*	2017	Marine Drugs	70	Extracts potential for treatment of DM through PTP1B and α-glucosidase inhibition.	[58]
44	Anusree Maneesh, Kajal Chakraborty	Previously Undescribed Fridooleanenes and Oxygenated Labdanes from the Brown Seaweed *Sargassum wightii* and Their Protein Tyrosine Phosphatase-1B inhibitory activity	2017	Phytochemistry	25	Fridooleanenes displayed significantly more excellent antioxidant and tyrosine phosphatase-1B inhibitory activities.	[59]
45	Kiana Pirian, Soheila Moein, Jelveh Sohrabipour, Reza Rabiei, Jaanika Blomster	Antidiabetic and antioxidant activities of brown and red macroalgae from the Persian Gulf	2017	Journal of Applied Phycology	57	α-amylase inhibition and the antioxidant effects.	[60]
46	Beibei Ren, Chun Chen, Chao Li, Xiong Fu, Lijun You, Rui Hai Liu	Optimization of Microwave-Assisted Extraction of *Sargassum thunbergii* Polysaccharides and its Antioxidant and Hypoglycemic Activities	2017	Carbohydrate Polymers	168	Polysaccharides extracted from *S. thunbergii* demonstrate the potential for use as potent antioxidants and agents capable of reducing blood sugar levels.	[61]
47	Jae-Eun Park, Ji-Hee Lee, Ji-Sook Han	*Sargassum yezoense* Extract Inhibits Carbohydrate Digestive Enzymes In Vitro and Alleviates Postprandial Hyperglycemia in Diabetic Mice	2017	Preventive Nutrition and Food Science	3	The ethanolic extract inhibits α-glucosidase and α-amylase activities, thereby delaying dietary carbohydrate absorption in the intestine.	[62]
48	Chengfeng Yang, Yuqing Chen, Mingjun Chen, Ruibo Jia, Bin Liu1, Chao Zhao	The Antidiabetic Activity of Brown Seaweed *Sargassum confusum* Polysaccharide Hydrolysates in Insulin Resistance HepG2 Cells in vitro	2017	Research Journal of Biotechnology	11	Polysaccharide hydrolysates from *S. confusum* have been discovered to effectively regulate blood glucose levels by diminishing the activity of α-glucosidase and enhancing insulin resistance.	[63]
49	T. Stalin Dhas, V. Ganesh Kumar, V. Karthick, K. Vasanth, G. Singaravelu, K. Govindaraju	Effect of biosynthesized gold nanoparticles by *Sargassum swartzii* in alloxan induced diabetic rats	2016	Enzyme and Microbial Technology	49	Enhanced secretion of insulin from the β-cells within the islets of Langerhans in the pancreas amplifies the insulin's effectiveness in the bloodstream.	[64]
50	Ji-Hyun Oh, Jaehoon Kim, Yunkyoung Lee	Anti-inflammatory and anti-diabetic effects of brown seaweeds in high-fat diet-induced obese mice	2016	Nutrition research and practice.	88	Supplementing a high-fat diet with *S. fulvellum* reduces inflammation without decreasing adipose depot mass and improves insulin resistance.	[65]
51	Amir Husni, Fajar Panji Anggara, Alim Isnansetyo, Agung Endro Nugroho	Blood Glucose Level and Lipid Profile of Streptozotozin-Induced Diabetic Rats Treated With *Sargassum polystum* Extract	2016	International Journal of Pharmaceutical and Clinical Research	22	The results showed that *S. polycystum* extract could prevent DM in rats induced by streptozotocin.	[66]
52	Amir Husni, Dwi Purwanti, Ustadi	Blood Glucose Level and Lipid Profile of Streptozotocin-induced Diabetes Rats Treated with Sodium Alginate from *Sargassum crassifolium*	2016	Journal of Biological Sciences	0	The present study demonstrates the potential antidiabetic action of alginate in STZ-induced diabetic rats.	[67]

53	S. Lakshmana Senthil, T. Vinoth Kumar, D. Geetharamani, G. Suja, Rincy Yesudas, Amrutha Chacko	Fucoidan – An α-amylase inhibitor from *Sargassum wightii* with relevance to NIDDM	2015	International Journal of Biological Macromolecules	28	Fucoidan from *S. wightii* also inhibits α-amylase	[68]
54	Yao Xian Chin, Phaik Eem Lim, Christine A. Maggs, Siew Moi Phang, Yusrizam Sharifuddin, Brian D. Green	Anti-diabetic potential of selected Malaysian seaweeds	2015	Journal of Applied Phycology	67	The potential therapeutic effects of *S. binderi* in managing T2DM may arise from its ability to inhibit crucial enzymes involved in diabetes.	[69]
55	Pai-An Hwang, Yu-Lan Hung, Yi-Kuan Tsai, Shih-Yung Chien, Zwe-Ling Kong	The brown seaweed *Sargassum hemiphyllum* exhibits α-amylase and α-glucosidase inhibitory activity and enhances insulin release in vitro	2015	Cytotechnology	65	The levels of polyphenols and fucoxanthin in the extracts directly correspond to the inhibition of α-amylase, α-glucosidase, sucrose, and maltase activities, as well as the stimulation of insulin secretion.	[70]
56	Mi Hwa Park, Young Hwa Nam, and Ji-Sook Han	*Sargassum coreanum* extract alleviates hyperglycemia and improves insulin resistance in db/db diabetic mice	2015	Nutrition Research and Practice	18	The extract from *S. coreanum* effectively lowers blood glucose concentration by modulating hepatic glucose metabolic enzyme activities and improving insulin resistance.	[71]
57	Nasrin Payghami, Shahla Jamili, Abdolhossein Rustaiyan, Soodabeh Saeidnia, Marjan Nikan, Ahmad Reza Gohari	Alpha-amylase inhibitory activity and sterol composition of the marine algae, *Sargassum glaucescens*	2015	Pharmacognosy Research	43	*S. glaucescens* exhibits strong inhibition of α-amylase activity in vitro.	[72]
58	T. Vinoth Kumar, S. Lakshmanasenthil, D. Geetharamani, T. Marudhupandi, G. Suja, P. Suganya	Fucoidan – A α-d-glucosidase inhibitor from *Sargassum wightii* with relevance to type 2 diabetes mellitus therapy	2015	International Journal of Biological Macromolecules	132	Fucoidan extracted from *S. wightii* displays significant inhibition of α-D-glucosidase.	[73]
59	Mahsa Motshakeri, Mahdi Ebrahimi, Yong Meng Goh, Hemn Hassan Othman, Mohd Hair-Bejo, Suhaila Mohamed	Effects of Brown Seaweed (*Sargassum polycystum*) Extracts on Kidney, Liver, and Pancreas of Type 2 Diabetic Rat Model	2014	Evidence-based complementary and alternative medicine	97	The extracts relieved liver and kidney damage in diabetic rats, suggesting potential tissue repair or restoration of pancreatic islets in experimentally induced diabetes.	[74]
60	Stalin Selvaraj, Sampathkumar Palanisamy,	Investigations on the anti-diabetic potential of novel marine seaweed *Sargassum longiotom* against alloxan-induced diabetes mellitus: A pilot study	2014	Bangladesh Journal of Pharmacology	14	The ethanolic extract of *S. longiotom* exhibited notable hypoglycemic and hypolipidemic effects.	[75]
61	Mahsa Motshakeri, Mahdi Ebrahimi, Yong Meng Goh, Patricia Matanjun, Suhaila Mohamed	*Sargassum polycystum* reduces hyperglycaemia, dyslipidaemia and oxidative stress via increasing insulin sensitivity in a rat model of type 2 diabetes	2013	Journal of the Science of Food and Agriculture	82	*S. polycystum* shows potential as an insulin sensitizer, offering a dietary supplement option for managing T2DM.	[76]
62	Chae-Won Lee, Ji-Sook Han	Hypoglycemic Effect of *Sargassum ringgoldianum* Extract in STZ-induced Diabetic Mice	2012	Preventive nutrition and food science.	39	The extract's suppression of α-glucosidase and α-amylase activities resulted in lowered blood glucose levels, effectively mitigating postprandial hyperglycemia..	[77]
63	Su-Nam Kim, Woojung Lee, Gyu-Un Bae, Yong Kee Kim	Anti-diabetic and hypolipidemic effects of *Sargassum yezoense* in db/db mice	2012	Biochemical and Biophysical	39	The extract enhances glucose and lipid metabolism, ameliorating metabolic	[78]

				Research Communications		disorders by activating PPARα and PPARγ without inducing notable adverse effects like hepatomegaly and weight gain.	
64	Su-Nam Kim, Hye Young Choi, Woojung Lee, Gab Man Park, Woon Seob Shin, Yong Kee Kim	Sargaquinoic acid and sargahydroquinoic acid from *Sargassum yezoense* stimulate adipocyte differentiation through PPARα/γ activation in 3T3-L1 cells	2008	FEBS Letters	99	Treatment with SQA and SHQA promoted adipocyte differentiation and upregulated the expression of key adipogenic marker genes such as PPARγ, aP2, C/EBPα, resistin, adiponectin, and Glut4 in 3T3-L1 cells.	[17]

Abbreviations: acetyl-CoA carboxylase (ACC1); alanine aminotransferase (ALT); albumin (ALB); alkaline phosphatase (ALP); alkaline phosphatase (ALP); aspartate aminotransferase (AST); atherogenic index (AI); blood glucose (BG); blood urea nitrogen (BUN); blood urea nitrogen (BUN); Body weight (BW); catalase (CAT); c-jun N-terminal kinase (JNK); creatinine (Cr); diastolic blood pressure (DBP); dipeptidyl peptidase IV (DPP IV); fatty acid synthase (FAS); food intake (FI); forkhead box protein O1 (FOXO1); free fatty acid (FFA); gamma-glutamyl transferase (GGT); glucose transporter 2 (GLUT2); glucose transporter 4 (GLUT4); glucose-6-phosphatase (G6Pase); glutathione peroxidase (GSH-Px); glycogen synthase kinase-3 beta, (GSK-3 beta); glycosylated hemoglobin (HbA1c); heme oxygenase 1 (HO-1); hemoglobin (HB); hemoglobin A1c (HbA1c); hexokinase (HK); high-density lipoprotein cholesterol (HDL); high-sensitivity C-reactive protein (hs-CRP); insulin receptor substrate 1 (IRS-1); insulin tolerance test (ITT); Interleukin-6 (IL-6); low-density lipoprotein (LDL); malonic dialdehyde (MDA); NAD(P)H quinone dehydrogenase 1 (NQO1); nuclear factor erythroid 2–related factor 2 (Nrf2); nuclear factor-κ beta (NF-κB); oral glucose tolerance test (OGTT); peroxisome proliferator-activated receptors (PPARs); phosphoenolpyruvate carboxylase (PEPCK); phosphoinositide 3-kinase (PI3K); protein kinase B (PKB, or Akt); protein tyrosine phosphatase 1B (PTP1B); quantitative insulin sensitivity check index (QUICKI); serum glutamate pyruvate transaminase (SGPT); serum glutamic oxaloacetic transaminase (SGOT); sterol regulatory element binding proteins (SREBPs); superoxide dismutase (SOD); systolic blood pressure (SBP); total bile acid (TBA); total bilirubin (TB); total cholesterol (TC); total protein (TP); triglycerides (TG); tumor necrosis factor-α (TNF-α); Uric acid (UA); very-low-density lipoprotein (VLDL); water intake (WI).

Table 2. Most Impactful Countries, Productive Sources, Prominent Institutions and Influential Authors

No	Most Impactful Countries			Most Productive Sources		Most Prominent Institutions		Most Influential Authors		
	Country	Publication	Citation	Sources	Articles	Institutions	Articles	Author	Documents	Citations
1	China	16	886	International Journal of Biological Macromolecules	9	South China University of Technology	47	Chao Li	4	424
2	Korea	12	275	Preventive Nutrition and Food Science	5	Wenzhou University	23	Xiong Fu	4	377
3	India	8	114	Journal of Applied Phycology	3	Fujian Agriculture and Forestry University	14	Rui-Bo Jia	4	155
4	Iran	6	137	Biocatalysis and Agricultural Biotechnology	2	Universiti Putra Malaysia	11	Lianzhu Lin	4	155
5	Indonesia	5	47	Foods	2	Zhejiang University of Technology	10	Juan Wu	4	155
6	Egypt	2	72	Marine Drugs	2	Pusan National University	9	Mouming Zhao	4	155
7	Japan	2	30	Nutrients	2	Biodiversity Research Institute	8	Amir Husni	4	57
8	Malaysia	2	107	Nutrition Research and Practice	2	Brawijaya University	8	Ji-sook Han	4	56
9	Denmark	1	69	Algal Research	1	Bushehr University of Medical Sciences	8	Chun Chen	3	279
10	Portugal	1	9	Annales Pharmaceutiques Francaises	1	Pukyong National University	8	Changliang Cao	3	260

Table 3. Highlights of bibliographic coupling network analysis based on authors.

No	Cluster	Authors	Research Focus	Publication timelines
1	Cluster 1 (Red Nodes)	Yao Xian Chin, Brian D. Green, Phaik Eem Lim, Muhamad Firdaus, Ji-Sook	This research focuses on identifying bioactive compounds with hypoglycemic potential from various *Sargassum* species using screening techniques. Subsequently, the study evaluates the efficacy of selected *Sargassum* species, including *S.olygocystum, S. polycystum, S. sagamianum, S. yezoense, S. coreanum, S.ringgoldianum, S. hystrix, S. crassifolium, S. serratifolium, S. confusum,*	2008, 2012, 2015-2022

		Han, Amir Husni, Alim Isnansetyo, Ustadi, Hyeung-Rak Kim, Su-Nam Kim, Yong Kee Kim, Woojung Lee, Bin Liu, Chao Zhao, R. Emilin Renitta, Antony V. Samrot	*and S.tenerrimum*, in alleviating hyperglycemia and improving insulin resistance in diabeticanimal models through both in silico and in vivo approaches. Additionally, the underlying mechanisms of action will be explored, potentially including the inhibition of carbohydrate-digesting enzymes, modulation of NF-κB and IL-6 expression, activation of PPAR pathways, regulation of gut microbiota, and interaction with JNK- IRS1/PI3K signaling pathways.	
2	Cluster 2 (Green Nodes)	Changliang Cao, Chun Chen, Xiong Fu, Qiang Huang, Chao Li, D. Geetharamani, G. Suja, T. Vinoth Kumar,	This research focuses on a comprehensive investigation of the potential therapeutic effects of polysaccharides extracted from *Sargassum* species, particularly *S. pallidum* and *S. thunbergii*. Initially, we will characterize the physicochemical properties of *S.pallidum* polysaccharides. Additionally, extraction techniques, including sulphated modification and microwave-assisted aqueous two-phase extraction, will be optimized to maximize the yield of bioactive compounds. Subsequently, the in vitro and in vivo antioxidant and hypoglycemic activities of the extracted polysaccharides will be evaluated.	2015, 2017, 2019, 2023
3	Cluster 3 (Blue Nodes)	Rui-Bo Jia,, Zhao-Rong Li, Lianzhu Lin, Zhi-Rong, Baoguo Sun, Juan Wu, Mouming Zhao	This research focuses on comprehensively exploring the therapeutic effects of polysaccharides derived from *S. fusiforme*, particularly in managing diabetes mellitus and dyslipidemia. Initially, the structural characteristics of the polysaccharide fractions will be elucidated, including their composition, molecular weight, and linkage patterns. Subsequently, in vivo studies using type 2 diabetic rat models will be conducted to evaluate the hypoglycemic and hypolipidemic activities of the polysaccharides.	2021, 2020, 2022
4	**Cluster 4** (Light Green Nodes)	Kyung-Soo Chang, Young-Min Ham, Ho-Bong Hyun, Yong-Hwan Jung, Young-Hyeon Lee, Min-Ho Yeo	This study employs a two-pronged approach, utilizing both in vitro and in vivo experiments, to investigate the antidiabetic potential of *Sargassum* extracts. In vitro studies will evaluate the ability of the extracts to modulate cellular processes relevant to diabetes, such as glucose uptake, insulin sensitivity, and inflammation, using relevant cellular models. In vivo experiments will assess the effects of the extracts on body weight, serum glucose levels, and long-term systemic glucose regulation and metabolic parameters in Sprague-Dawley rats.	2021, 2023
5	**Cluster 5** (Purple Nodes)	Yang Cheng, Mingjiang Wu, Siya Wu, Yue Yang, Xu Zhang, Haibin Tong	This research comprehensively explores the therapeutic effects of various compounds extracted from *S. fusiforme*, including ethanol extract, alginate, and fucoidan, in the context of type 2 diabetes mellitus (T2DM). The study aims to elucidate how these compounds alleviate hyperglycemia, specifically focusing on their potential role in modulating gut microbiota and intestinal metabolites.his	2019, 2021
6	**Cluster 6** (Light Blue Nodes)	Mahdi Ebrahimi, Yong Meng Goh, Suhaila Mohamed, Mahsa Motshakeri	This research will comprehensively examine the impact of *S. polycystum* extracts on the kidney, liver, and pancreas in a type 2 diabetic rat model. The study seeks to evaluate the capacity of *S. polycystum* extracts to alleviate the adverse effects of diabetes on these crucial organs.	2013, 2014
7	**Cluster 7** (Orange Nodes)	Amir Reza Jassbi, Hossein Mirkhani, Jelveh Sohrabipour	This research explores the potential antidiabetic properties of macroalgae indigenous to the Persian Gulf. The study is specifically designed to assess the in vitro α-glucosidase inhibition and antibacterial activities of three brown algae (*Polycladia myrica, Padina antillarum*, and *Sargassum boveanum*) and one red alga (*Palisada perforata*). Furthermore, in vivo experiments using animal models of diabetes will be conducted to evaluate these macroalgae's antidiabetic and antioxidant activities.	2017, 2022, 2023

Table 4. Cited reference-based co-citation network highlights

No	Cluster	Authors	Title	Year	Cluster themes	Description themes	Reference
1	Cluster 1 (red nodes)	Markolf Hanefeld	The role of acarbose in the treatment of non–insulin-dependent diabetes mellitus.	1998	Exploring Natural Compounds for Diabetes Management	This topic investigates the potential of natural compounds in managing DM. Studies include the effects of acarbose on NIDDM, the discovery of phlorotannins from brown algae as carbohydrate-hydrolyzing enzyme inhibitors, the impact of Rhemanniae radix on hyperglycemic mice, the adipocyte differentiation stimulation by sargaquinoic and sargahydroquinoic acids from *S. yezoense*, the apoptosis-inducing properties of porphyran in gastric cancer cells, and the diabetes-ameliorating effects of *Ishige okamurae* in mice.	[79]
2		Yasuko Kawamura-Konishi, Natsuko Watanabe, Miki Saito, Noriyuki Nakajima, Toshiyuki Sakaki, Takane Katayama, Toshiki Enomoto	Isolation of a new phlorotannin, a potent inhibitor of carbohydrate-hydrolyzing enzymes, from the brown alga *Sargassum patens.*	2012			[80]
3		Kim JS.	Effect of *Rhemanniae radix* on the hyperglycemic mice induced with streptozotocin.	2004			[81]
4		Su-Nam Kim, Hye Young Choi, Woojung Lee, Gab Man	Sargaquinoic acid and sargahydroquinoic acid from *Sargassum yezoense* stimulate	2008			[17]

		Park, Woon Seob Shin, Yong Kee Kim	adipocyte differentiation through PPARα/γ activation in 3T3-L1 cells.				
5		Mi-Jin Kwon, Taek-Jeong Nam	Porphyran induces apoptosis related signal pathway in AGS gastric cancer cell lines.	2006			[82]
6		Kwan-Hee Min, Hak-Ju Kim, You-Jin Jeon, Ji-Sook Han	*Ishige okamurae* ameliorates hyperglycemia and insulin resistance in C57BL/KsJ-*db/db* mice.	2011			[83]
7		Wickramaarachchilage Anoja Pushpamali, Chamilani Nikapitiya, Mahanama De Zoysa, Ilson Whang, Se Jae Kim, Jehee Lee	Isolation and purification of an anticoagulant from fermented red seaweed *Lomentaria catenata.*	2008			[84]
8		Jun Watanabe, Jun Kawabata, Hideyuki Kurihara, Ryoya Niki	Isolation and identification of α-glucosidase inhibitors from tochu-cha (*Eucommia ulmoides*).	1997			[85]
9	Cluster 2 (green nodes)	Soo-Jin Heo, Eun-Ju Park, Ki-Wan Lee, You-Jin Jeon	Antioxidant activities of enzymatic extracts from brown seaweeds.	2005	Exploring the Health Benefits of Marine Algae	This topic explores the multifaceted health-promoting attributes of marine algae. Research encompasses the antioxidant activities of enzymatic extracts from brown seaweeds, the correlation between obesity and health, the nutritional significance of edible seaweeds, the anti-proliferative and potential anti-diabetic effects of phenolic-rich extracts from marine algae, the therapeutic relevance of sulfated polysaccharides from seaweeds, and the inhibition of liver lipid peroxidation by high molecular weight phlorotannins from *S. kjellmanianum*.	[86]
10		Peter G. Kopelman	Obesity as a medical problem.	2000			[87]
11		Paul MacArtain, Christopher I.R. Gill, Mariel Brooks, Ross Campbell, Ian R. Rowland	Nutritional value of edible seaweeds. Nutrition reviews.	2007			[88]
12		Felix Nwosu, Jennifer Morris, Victoria A. Lund, Derek Stewart, Heather A. Ross, Gordon J. McDougall	Anti-proliferative and potential anti-diabetic effects of phenolic-rich extracts from edible marine algae.	2011			[89]
13		Seema Patel	Therapeutic importance of sulfated polysaccharides from seaweeds: updating the recent findings.	2012			[90]
14		Yuxi Wei, Zhi'en Li, Yingfen Hu, Zuhong Xu	Inhibition of mouse liver lipid peroxidation by high molecular weight phlorotannins from *Sargassum kjellmanianum.*	2003			[91]
15	Cluster 3 (blue-nodes)	World Health Organization	WHO Global report on diabetes	2016	Advancements in Diabetes Research: From Global Insights to Novel Therapeutic Targets	This topic explores various facets of diabetes, ranging from global epidemiological insights provided by the WHO Global Report on Diabetes to the discovery of novel drug targets for type 2 diabetes and metabolic syndrome. It involves the exploration of new antidiabetic agents, such as the N-trisaccharide isolated from *Cucumis prophetarum*, and the investigation of targets for intervening in dyslipidemia associated with diabetes. Additionally, it examines the potential antidiabetic properties of natural substances, particularly fractions enriched with polysaccharides and polyphenols derived from the brown seaweed *Ascophyllum nodosum.*	[92]

16		G.B. Kavishankar, N. Lakshmidevi	Anti-diabetic effect of a novel N-Trisaccharide isolated from *Cucumis prophetarum* on streptozotocin–nicotinamide induced type 2 diabetic rats.	2014			[93]
17		David E. Moller	New drug targets for type 2 diabetes and the metabolic syndrome	2001			[94]
18		Gerald H. Tomkin,	Targets for intervention in dyslipidemia in diabetes.	2008			[95]
19		Junzeng Zhang, Christa Tiller, Jingkai Shen, Can Wang, Gabrielle S. Girouard, Dorothy Dennis, Colin J. Barrow, Mingsan Miao, H. Stephen Ewart	Antidiabetic properties of polysaccharide-and polyphenolic-enriched fractions from the brown seaweed *Ascophyllum nodosum.*	2007			[96]
20	Cluster 4 (yellow-nodes),	Yuto Kamei, Chi Kwan Tsang	Sargaquinoic acid promotes neurite outgrowth via protein kinase A and MAP kinases-mediated signaling pathways in PC12D cells.	2003	Harnessing the Therapeutic Potential of Brown Seaweeds for Diabetes Management	This extensive subject explores the diverse therapeutic characteristics of brown seaweeds for diabetes. The research investigates different approaches, such as the stimulation of neurite outgrowth by sargaquinoic acid in PC12D cells, the effects of *S. yezoense* on reducing diabetes and lowering lipid levels in db/db mice, and the various mechanisms responsible for the anti-diabetic effects of phlorotannins, which are marine polyphenols obtained from brown algae. Furthermore, it offers a comprehensive analysis of the phytochemical and pharmacological properties of the brown seaweed *Sargassum*, shedding light on its traditional medicinal applications in Traditional Chinese Medicine. Moreover, it explores how alloxan and streptozotocin affect the B cells in the pancreas of rats, thus enhancing our comprehension of the pathophysiology of diabetes.	[97]
21		Su-Nam Kim, Woojung Lee, Gyu-Un Bae, Yong Kee Kim	Anti-diabetic and hypolipidemic effects of *Sargassum yezoense* in db/db mice.	2012			[78]
22		Seung-Hong Lee, You-Jin Jeon	Anti-diabetic effects of brown algae derived phlorotannins, marine polyphenols through diverse mechanisms.	2013			[98]
23		Lei Liu, Michael Heinrich, Stephen Myers, Symon A. Dworjanyn	Towards a better understanding of medicinal uses of the brown seaweed *Sargassum* in Traditional Chinese Medicine: A phytochemical and pharmacological review.	2012			[99]
24		T Szkudelski	The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas.	2001			[100]
25	Cluster 5 (purple-nodes)	Shilpi Gupta, Nissreen Abu-Ghannam	Bioactive potential and possible health effects of edible brown seaweeds.	2011	Exploring the Health Benefits of Brown Seaweeds: From Bioactive Compounds to Potential Therapeutic Effects	This study thoroughly investigates edible brown seaweeds' bioactive properties and potential health effects. The text discusses several study findings, such as the ability of phlorotannins found in Alaskan seaweed to block carbolytic enzyme activity and the identification of meroditerpenoids from the marine brown alga *S. fallax* in southern Australia. This study provides an in-depth analysis of the many bioactive chemicals found in brown seaweeds and their potential therapeutic uses. It offers valuable information about how these compounds contribute to improving human health and overall well-being.	[101]
24		Joshua Kellogg, Mary H. Grace, Mary Ann Lila	Phlorotannins from Alaskan seaweed inhibit carbolytic enzyme activity	2014			[102]
27		Priyanka Reddy, Sylvia Urban	Meroditerpenoids from the southern Australian marine brown alga *Sargassum fallax.*	2009			[103]

3.4 Analysis of prominent institutions

The analysis of 64 articles revealed that 78 institutions were involved in preclinical research on the antidiabetic properties of *Sargassum*. South China University of Technology is the most prominent institution with the most articles. Most of these institutions are based in Asia (Table 2- Most Prominent Institutions).

3.5 Analysis of authors and bibliographical coupling network

During the study period, bibliographic data from 64 selected documents was inputted into VOSviewer to construct a network of authors through bibliographic coupling, a method that analyses how often authors cite the same references. This analysis identified 270 authors who investigated the preclinical antidiabetic activities of *Sargassum*. The network focused on the most influential authors, defined as those with at least four publications each (eight authors: Chao Li, Xiong Fu, Rui-Bo Jia, Lianzhu Lin, Juan Wu, Mouming Zhao, Amir Husni, Ji-sook Han) (Table 2- Most Influential Authors). Among these, Chao Li emerged as the most influential author with four publications and 424 citations. The VOSviewer algorithm mapped and clustered the authors's bibliographic coupling network. The author's bibliographic coupling network was mapped using the VOSviewer algorithm and clustered according to subject relatedness, where the distance between nodes directly reflects their thematic proximity. The thickness of the connecting lines represents the intensity of bibliographic coupling between nodes. Following the application of mapping and clustering algorithms, the resulting visualization of the author's bibliographic coupling network is presented in Figure 4. Researchers, academic entities, and nations will offer valuable perspectives to facilitate further scholarly development and foster collaborative research efforts. Additionally, a method called author-based bibliographical coupling was introduced, which examines the citation patterns of authors who reference similar articles in their works [104].

Fig. 4. Author-based bibliographic coupling network

To construct a meaningful co-citation network, a minimum publication threshold was established for author inclusion. With a minimum of two documents per author, 50 authors out of 270 were identified, representing a balance between network size and author expertise. Lowering the threshold to one document yielded the most extensive network (268 authors), but this risked including less influential authors. Conversely, raising the threshold to three documents resulted in a network with only 16 authors, deemed insufficient for meaningful analysis. Therefore, a two-document minimum was chosen, resulting in a network with 50 authors, 635 links, and a total link strength of 11979. This network size reflects a robust level of author coupling within the cluster, suggesting a high degree of overlap in cited references. Further details regarding the network analysis, including the identification of seven distinct clusters, are presented in Table 3.

3.6 Analysis of the most impactful articles and co-citation network

The most influential publications were identified based on their total citation count. Table 1 presents the total citations for each analyzed journal article. The award-winning research by Beibei Ren et al. (2017), titled "Optimization of Microwave-Assisted Extraction of *Sargassum thunbergii* Polysaccharides and its Antioxidant and Hypoglycemic Activities", emerged as the most cited publication [61]. The remaining nine highly influential articles all investigated themes related to 'Exploring the Antioxidant, Hypoglycemic, and Gut Microbiota Modulation Properties of *Sargassum*-Derived Polysaccharides and Bioactive Compounds in Diabetes Management'.

Co-citation network analysis is a valuable tool for exploring the intellectual structure and knowledge development within a scientific field [105]. This technique identifies frequently co-cited documents, indicating a strong thematic connection and highlighting influential research areas [106]. By analyzing co-citation patterns, we can measure the semantic similarity between documents, with a higher co-citation frequency suggesting a stronger conceptual link [9] [105]. Co-citation analysis examines document citation patterns to measure their semantic similarity. A larger number of co-citations indicates a stronger semantic connection [105]. In this study, co-citation network analysis was employed to investigate the scholarly impact of researchers in the field and to visualize the thematic relationships between highly cited articles [9].

Constructing a meaningful co-citation network requires a balance between network size and the expertise of included documents. A minimum threshold of three citations resulted in only 12 documents, deemed insufficient. Conversely, including all 2653 documents satisfying the one-citation threshold led to software limitations excluding unconnected items. Therefore, a two-citation threshold was chosen, yielding a network with 72 documents. While not all documents are interconnected, the largest connected component comprised 27 documents, further analyzed for thematic relationships. Five clusters were identified (Figure 5): cluster 1 (red), cluster 2 (green), cluster 3 (blue), cluster 4 (yellow), and cluster 5 (purple), containing 8, 6, 5, 5, and 3 documents, respectively. Circle size represents the number of citations a document receives, and the distance between circles reflects thematic similarity [9]. These findings highlight the potential of marine algae as a source of novel therapeutic and nutritional interventions for diabetes and related disorders, emphasizing the need for further exploration of their bioactive properties for the sake of human health. Detailed network analysis results are presented in Table 4.

Fig. 5. Co-citation network of cited references

3.7 Analysis of keyword co-occurrence network

Co-occurrence network analysis with overlay techniques can efficiently identify emerging research domains by providing unbiased and reproducible insights into core topics of investigation. To achieve this, keywords and their co-occurrences are extracted from titles, abstracts, and author-provided keywords within a publication set. The resulting network visualization depicts nodes representing keywords connected by edges, where edge thickness signifies the strength of association between terms and node size reflects keyword frequency. Additionally, overlapping nodes indicate frequent co-occurrence within the network [9] [107]. This study constructed a keyword co-occurrence network based on text data extracted from titles and abstracts in a bibliographic database. A minimum threshold of 10 occurrences was applied to the 1807 terms identified, resulting in 32 keywords for network analysis. The visualization revealed two distinct clusters, as shown in Figure 6.

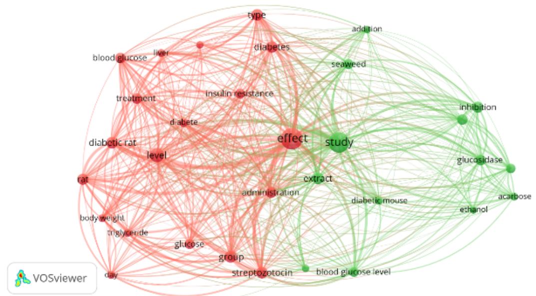


Fig. 6. Keyword co-occurrence network

Cluster 1 (red node) encompasses 31 keywords, including administration, blood glucose, body weight, day, diabetes (various terms), diabetic rat, effect, glucose, group, insulin resistance, level, liver, rat, streptozotocin, treatment, and triglyceride. This cluster highlights research centered on the effects of treatment interventions on streptozotocin-induced diabetic rats. Key areas of investigation include blood glucose level regulation, body weight changes, and insulin resistance. Specifically, it investigates the effects of treatment on blood glucose levels, body weight changes, and insulin resistance. Through experimental manipulation and group comparisons, the study aims to elucidate the therapeutic potential of interventions in managing diabetes mellitus and associated metabolic dysregulations, with a focus on glucose metabolism, liver function, and triglyceride levels.

Cluster 2 (green node) centers on 13 keywords, including acarbose, amylase, blood glucose level, diabetic mouse, ethanol extract, glucosidase, inhibition, *Sargassum*, seaweed, in vitro study. This cluster focuses on research investigating the potential synergistic effects of combining acarbose with *Sargassum* seaweed extract on glucosidase inhibition and blood glucose regulation in diabetic mice, specifically within an in vitro setting. These studies aim to elucidate the mechanisms underlying the interventions' impact on blood sugar control by assessing amylase and glucosidase activity.

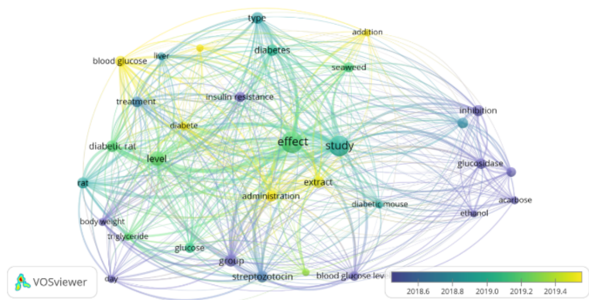


Fig. 7. Keyword co-occurrence overlay with a time frame.

Figure 7 presents a keyword co-occurrence map alongside a timeline. Node size reflects keyword frequency, with larger nodes indicating more frequent occurrences. The color gradient represents the average publication year for articles containing the keyword, where purple signifies publications before or around 2018.6, purple-blue around 2018.8, blue-green around 2019.0, green around 2019.2, and yellow around or after 2019.4 [9]. By exploring the therapeutic potential of *Sargassum* extract, the study seeks to provide insights into novel strategies for diabetes management and glycemic control. These findings highlight the growing research interest in *Sargassum* extract as a potential therapeutic strategy for diabetes management and glycemic control.

4 Conclusion

Sargassum has emerged as a promising therapeutic agent for diabetes management. This study presents the first bibliometric analysis of preclinical studies investigating *Sargassum*'s antidiabetic properties. Publication output on this topic fluctuated between 2008 and 2023. Notably, China emerged as the most productive country. At the same time, South China University of Technology, the International Journal of Biological Macromolecules, Chao Li (author), and the research by Beibei Ren stood out as the leading institution, source journal, prominent author, and most impactful article, respectively. These findings illuminate key trends in *Sargassum* research. Future investigations should focus on identifying pharmacological markers, establishing effective dosages for human applications, and advancing formulation technologies to optimize therapeutic potential.

We express our gratitude to the Indonesian Education Scholarship and the Ministry of Education, Culture, Research, and Technology of the Republic of Indonesia for providing funding with BPI Identification Number 202209090572.

References

1. Lee J. E., Jeon H.-J., Lee O.-J., Lim H. G., Diagnosis of diabetes mellitus using high frequency ultrasound and convolutional neural network. Ultrasonics. **136**, 107167 (2024).
2. Sun H., Saeedi P., Karuranga S., Pinkepank M., Ogurtsova K., Duncan B.B., Stein C., Basit A., Chan J.C., Mbanya J.C., Pavkov, M.E, IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res. Clin. Pract. **183**, 109119 (2022).
3. Attaallah R., Elfadil D., Amine A., Screening study of enzymatic inhibition of medicinal plants for the treatment of diabetes using a glucometer biosensor approach and optical method. J. Herb. Med. **28**, 100441 (2021).
4. Rohman A., Arifah F. H., Alam G., Rafi M., A review on phytochemical constituents, role on metabolic diseases, and toxicological assessments of underutilized part of G*arcinia mangostana* L. fruit. J. Appl. Pharm. Sci. **10**, 127–146 (2020).
5. Xie X., Chen C., Fu X., Modulation Effects of *Sargassum pallidum* Extract on Hyperglycemia and Hyperlipidemia in Type 2 Diabetic Mice. Foods. **12**, (2023).
6. Puhari S. S. M. et al. Fucoidan from *Sargassum wightii* reduces oxidative stress through upregulating Nrf2/HO-1 signaling pathway in alloxan-induced diabetic cardiomyopathy rats. Mol. Biol. Rep. **50**, 8855–8866 (2023).
7. Paramasivam D., et al. Marine brown algae (*Sargassum wightii*) derived 9-hydroxyhexadecanoic acid: A promising inhibitor of α-amylase and α-glucosidase with mechanistic insights from molecular docking and its non-target toxicity analysis. *South* African J. Bot. **161**, 627–637 (2023).
8. Lee Y.-H., et al. Anti-Diabetic Potential of Sargassum horne*ri* and *Ulva australis* Extracts In Vitro and In Vivo. Curr. Issues Mol. Biol. **45**, 7492–7512 (2023).
9. Bamel U. K., Pandey R., Gupta A., Safety climate: Systematic literature network analysis of 38 years (1980-2018) of research. Accid. Anal. Prev. **135**, 105387 (2020).
10. Yeung A. W. K., Heinrich M., Atanasov, A. G., Ethnopharmacology—a bibliometric analysis of a field of research meandering between medicine and food science. Front. Pharmacol. **9**, 215 (2018).
11. Elisha I. L., Viljoen A., Trends in Rooibos Tea (Aspalathus linearis) research (1994–2018): A scientometric assessment. South African J. Bot. **137**, 159–170 (2021).
12. Samudra A. G., Nugroho, A. E., Murwanti, R., Review of the pharmacological properties of marine macroalgae used in the treatment of diabetes mellitus in Indonesia. in Annales Pharmaceutiques Françaises (Elsevier, 2024).
13. Yu Y., et al. A bibliometric analysis using VOSviewer of publications on COVID-19. Ann. Transl. Med. **8**, 816 (2020).
14. Aria M., Cuccurullo C., bibliometrix: An R-tool for comprehensive science mapping analysis. J. Informetr. **11**, 959–975 (2017).
15. Ramamoorthi R., Gahreman D., Skinner T., Moss S., Bibliometric Profile and Density Visualizing Analysis of Yoga Intervention in Type 2 Diabetes: A 44 - Year Study on Global Scientific Research Output from 1975 to 2019. Int. J. Yoga. **14**, 89–99 (2021).
16. Yeung A. W. K., Mocan A., Atanasov A. G., Let food be the medicine and medicine be the food: A bibliometric analysis of the most cited papers focusing on nutraceuticals and functional foods. Food Chem. **269**, 455–465 (2018).
17. Kim S.N., et al. Sargaquinoic acid and sargahydroquinoic acid from *Sargassum* yezoense stimulate adipocyte differentiation through PPARα/γ activation in 3T3-L1 cells. FEBS Lett. **582**, 3465–3472 (2008).
18. Husni A., Pratiwi T., Samudra A. G., Nugroho A. E., In vitro antidiabetic activity of Sargassum

hystrix and *Eucheuma denticulatum* from Yogyakarta Beach of Indonesia: Antidiabetic activity of *S. hystrix* and *E. denticulatum*. Proc. Pakistan Acad. Sci. B. Life Environ. Sci. **55**, 1–8 (2018).
19. Raji V., Loganathan C., Ramesh T., Thayumanavan P., Dual antidiabetic and antihypertensive activity of fucoxanthin isolated from *Sargassum wightii* Greville in in vivo rat model. Food Sci. Hum. Wellness. **12**, 1693–1700 (2023).
20. Liu J., et al*., Sargassum fusiforme* alginate relieves hyperglycemia and modulates intestinal microbiota and metabolites in type 2 diabetic mice. Nutrients **13**, (2021).
21. Vijay N. K. G., Vellapandian C., Ameliorative effects of phlorotannin-rich fraction of *Sargassum tenerrimum* in high-fat diet and low dose streptozotocin-induced metabolic changes and oxidative stress in diabetic rats. J. HerbMed Pharmacol. **12**, 367–379 (2023).
22. Samudra A. G., *et al.*, Antihyperglycemic activity of nanoemulsion of brown algae (*Sargassum* sp.). Ethanol extract in glucose tolerance test in male mice. Ann. Pharm. *Fr.* **81**, 484–491 (2023).
23. Gheda S., *et al.,* Potent Effect of Phlorotannins Derived from *Sargassum linifolium* as Antioxidant and Antidiabetic in a Streptozotocin-Induced Diabetic Rats Model. Appl. Sci. **13**, (2023).
24. Moheimanian N., Mirkhani H., Purkhosrow A., Sohrabipour J., Jassbi A. R., In Vitro and In Vivo Antidiabetic, α-Glucosidase Inhibition and Antibacterial Activities of Three Brown Algae, *Polycladia myrica*, *Padina antillarum*, and *Sargassum boveanum*, and a Red Alga, *Palisada perforata* from the Persian Gulf. *Iran.* J. Pharm. Res. **22**, (2023).
25. Park J.-W., Kang K. S., Ha I. S., Lee S. I., Shin S., Efficacy of fucoxanthin extract from *Sargassum horneri* on 3T3-L1 pre-adipocyte differentiation. Cell. Mol. Biol. **69**, 8–11 (2023).
26. Arguelles E. D., Preliminary Studies on the Potential Antioxidant and Antidiabetic Activities of *Sargassum polycystum* C. Agardh (Phaeophyceae, Ochrophyta). Jordan J. Biol. *Sci.* **15**, 449–456 (2022).
27. Moheimanian N., Mirkhani H., Sohrabipour J., Jassbi, A. R., Inhibitory Potential of Six Brown Algae from the Persian Gulf on α-Glucosidase and In Vivo Antidiabetic Effect of Sirophysalis Trinodis. Iran. J. Med. Sci. **47**, 484–493 (2022).
28. Jia R.-B. et al., The Beneficial Effects of Two Polysaccharide Fractions from *Sargassum fusiform* against Diabetes Mellitus Accompanied by Dyslipidemia in Rats and Their Underlying Mechanisms. Foods **11**, (2022).
29. Un S. et al*.,* Effects of In Vitro Digestion on Anti-α-Amylase and Cytotoxic Potentials of *Sargassum* spp. Molecules. **27**, (2022).
30. Firdaus M. et al., The glucose uptake of type 2 diabetic rats by *Sargassum olygocystum* extract: In silico and in vivo studies. J. Appl. Pharm. Sci. **12**, 132–139 (2022).
31. Zhang M., Yang R., Yu S., Zhao W., A novel α-glucosidase inhibitor polysaccharide from *Sargassum fusiforme*. Int. J. Food Sci. Technol. **57**, 67–77 (2022).
32. Lindsey A. et al., Evaluation of Antidiabetic Activity of *Sargassum tenerrimum* in Streptozotocin-Induced Diabetic Mice. *J. Pure Appl. Microbiol.* **15**, (2021).
33. Barbosa M., Fernandes F., Carlos M. J., Valentão P., Andrade P. B., Adding value to marine invaders by exploring the potential of *Sargassum muticum* (Yendo) Fensholt phlorotannin extract on targets underlying metabolic changes in diabetes. Algal Res. **59**, (2021).
34. Wu S., et al., Ethanol extract of *Sargarsum fusiforme* alleviates HFD/STZ-induced hyperglycemia in association with modulation of gut microbiota and intestinal metabolites in type 2 diabetic mice. Food Res. Int. **147**, (2021).
35. Oliyaei N., Moosavi-Nasab M., Tamaddon A. M., Tanideh N., Antidiabetic effect of fucoxanthin extracted from *Sargassum angustifolium* on streptozotocin-nicotinamide-induced type 2 diabetic mice. Food Sci. Nutr. **9**, 3521–3529 (2021).
36. Li Z.-R., et al., *Sargassum fusiforme* polysaccharide partly replaces acarbose against type 2 diabetes in rats. Int. J. Biol. Macromol. **170**, 447–458 (2021).
37. Murakami S. et al., The edible brown seaweed *Sargassum horneri* (Turner) C. agardh ameliorates high-fat diet-induced obesity, diabetes, and hepatic steatosis in mice. Nutrients**.** **13**, 1–14 (2021).
38. Lee Y.-H., et al., Effects of *Sargassum horneri* and *Ulva australis* extracts on body weight and serum glucose levels of sprague-dawley rats. Prev. Nutr. Food Sci. **26**, 307–314 (2021).
39. Renitta R. E., Narayanan R., Cypriyana P.J., Samrot A. V., Antidiabetic potential of methanolic extracts of *Sargassum wightii* in streptozotocin induced diabetic mice. Biocatal. Agric. Biotechnol. **28**, (2020).
40. Jia R.-B., et al., Structural characterization of polysaccharides from three seaweed species and their hypoglycemic and hypolipidemic activities in type 2 diabetic rats. Int. J. Biol. Macromol. **155**, 1040–1049 (2020).
41. Jia R.B., et al., Physicochemical properties of polysaccharide fractions from *Sargassum fusiforme* and their hypoglycemic and hypolipidemic activities in type 2 diabetic rats. Int. J. Biol. Macromol. **147**, 428–438 (2020).
42. Wei B., et al., *Sargassum fusiforme* polysaccharides prevent high-fat diet-induced early fasting hypoglycemia and regulate the gut microbiota composition. Mar. Drugs. **18**, (2020).
43. Nasab S. B., Homaei A., Karami, L., Kinetic of α-amylase inhibition by Gracilaria corticata and *Sargassum angustifolium* extracts and zinc oxide nanoparticles. Biocatal. Agric. Biotechnol. **23**, (2020).
44. Chin Y. X. *et al.* Characterization of seaweed hypoglycemic property with integration of virtual

screening for identification of bioactive compounds. J. Funct. Foods. **64**, (2020).
45. Ismail, G. A., Gheda, S. F., Abo-Shady, A. M., Abdel-Karim, O. H. In vitro potential activity of some seaweeds as antioxidants and inhibitors of diabetic enzymes. Food Sci. Technol. **40**, 681–691 (2019).
46. Cao, C. *et al.* Physicochemical characterization, potential antioxidant and hypoglycemic activity of polysaccharide from *Sargassum pallidum*. Int. J. Biol. Macromol. **139**, 1009–1017 (2019).
47. Yang, C.-F. *et al.* Anti-diabetic effect of oligosaccharides from seaweed *Sargassum confusum* via JNK-IRS1/PI3K signalling pathways and regulation of gut microbiota. Food Chem. Toxicol. **131**, (2019).
48. Cheng, Y. *et al. Sargassum fusiforme* fucoidan modifies the gut microbiota during alleviation of streptozotocin-induced hyperglycemia in mice. *Int.* J. Biol. Macromol. **131**, 1162–1170 (2019).
49. Xiao, H. *et al.* Sulfated modification, characterization, antioxidant and hypoglycemic activities of polysaccharides from *Sargassum pallidum*. Int. J. Biol. Macromol. **121**, 407–414 (2019).
50. Gotama, T. L., Husni, A. Antidiabetic activity of *Sargassum hystrix* extracts in streptozotocin-induced diabetic rats. Prev. Nutr. Food Sci. **23**, 189–195 (2018).
51. Lee, J.-S., Han, J.-S. *Sargassum sagamianum* extract alleviates postprandial hyperglycemia in diabetic mice. Prev. Nutr. Food Sci. **23**, 122–126 (2018).
52. Nurfahmi, A. R., Husni, A., Isnansetyo, A. Effect of *Sargassum* hystrix powder on the biochemical profile of diabetic wistar rats. Pakistan J. Nutr. **17**, 248–254 (2018).
53. Zaharudin, N., Salmeán, A. A., Dragsted, L. O. Inhibitory effects of edible seaweeds, polyphenolics and alginates on the activities of porcine pancreatic α-amylase. Food Chem. **245**, 1196–1203 (2018).
54. Cao, C., Huang, Q., Zhang, B., Li, C., Fu, X. Physicochemical characterization and in vitro hypoglycemic activities of polysaccharides from *Sargassum* pallidum by microwave-assisted aqueous two-phase extraction. Int. J. Biol. Macromol. **109**, 357–368 (2018).
55. Akbarzadeh, S. *et al.* Anti-diabetic effects of *Sargassum* oligocystum on Streptozotocin-induced diabetic rat. Iran. J. Basic Med. Sci. **21**, 342–346 (2018).
56. Kwon, M., Lim, S.-J., Lee, B., Shin, T., Kim, H.-R. Ethanolic extract of *Sargassum* serratifolium inhibits adipogenesis in 3T3-L1 preadipocytes by cell cycle arrest. J. Appl. Phycol. **30**, 559–568 (2018).
57. Firdaus, M., Chamidah, A. *Sargassum* polycystum methanol extract affects the nuclear factor-k beta and interleukin-6 expression in streptozotocin-induced diabetes rats. Asian J. Pharm. Clin. Res. **11**, 337–339 (2018).
58. Ali, Y. *et al.* α-Glucosidase and protein tyrosine phosphatase 1b inhibitory activity of plastoquinones from marine brown alga *Sargassum* serratifolium. Mar. Drugs. **15**, (2017).
59. Maneesh, A., Chakraborty, K. Previously undescribed fridooleanenes and oxygenated labdanes from the brown seaweed *Sargassum* wightii and their protein tyrosine phosphatase-1B inhibitory activity. Phytochemistry **144**, 19–32 (2017).
60. Pirian, K., Moein, S., Sohrabipour, J., Rabiei, R., Blomster, J. Antidiabetic and antioxidant activities of brown and red macroalgae from the Persian Gulf. J. Appl. Phycol. **29**, 3151–3159 (2017).
61. Ren, B. *et al.* Optimization of microwave-assisted extraction of *Sargassum* thunbergii polysaccharides and its antioxidant and hypoglycemic activities. Carbohydr. Polym. **173**, 192–201 (2017).
62. Park, J.-E., Lee, J.-H., Han, J.-S. *Sargassum yezoense* extract inhibits carbohydrate digestive enzymes in vitro and alleviates postprandial hyperglycemia in diabetic mice. Prev. Nutr. Food Sci. **22**, 166–171 (2017).
63. Yang, C. *et al.* The antidiabetic activity of brown seaweed *Sargassum confusum* polysaccharide hydrolysates in insulin resistance HepG2 cells in vitro. Res. J. Biotechnol. **12**, 1–9 (2017).
64. Dhas, T. S. *et al.* Effect of biosynthesized gold nanoparticles by *Sargassum swartzii* in alloxan induced diabetic rats. Enzyme Microb. Technol. **95**, 100–106 (2016).
65. Oh, J.-H., Kim, J., Lee, Y. Anti-inflammatory and anti-diabetic effects of brown seaweeds in high-fat diet-induced obese mice. Nutr. Res. Pract. **10**, 42–48 (2016).
66. Husni, A., Anggara, F. P., Isnansetyo, A., Nugroho, A. E. Blood glucose level and lipid profile of streptozotozin-induced diabetic rats treated with *Sargassum polystum* extract. Int. J. Pharm. Clin. Res. **8**, 445–450 (2016).
67. Husni, A., Purwanti, D., Ustadi. Blood Glucose Level and Lipid Profile of Streptozotocin-induced Diabetes Rats Treated with Sodium Alginate from *Sargassum crassifolium*. J. Biol. Sci. **16**, 58–64 (2016).
68. Lakshmana Senthil, S. *et al.* Fucoidan - An α-amylase inhibitor from *Sargassum wightii* with relevance to NIDDM. Int. J. Biol. Macromol. **81**, 644–647 (2015).
69. Chin, Y. X. *et al.* Anti-diabetic potential of selected Malaysian seaweeds. J. Appl. Phycol. **27**, 2137–2148 (2015).
70. Hwang, P.-A., Hung, Y.-L., Tsai, Y.-K., Chien, S.-Y., Kong, Z.-L. The brown seaweed *Sargassum hemiphyllum* exhibits α-amylase and α-glucosidase inhibitory activity and enhances insulin release in vitro. Cytotechnology. **67**, 653–660 (2015).
71. Park, M. H., Nam, Y. H., Han, J.-S. *Sargassum coreanum* extract alleviates hyperglycemia and improves insulin resistance in db/db diabetic mice. Nutr. Res. Pract. **9**, 472–479 (2015).
72. Payghami, N. *et al.* Alpha-amylase inhibitory

activity and sterol composition of the marine algae, Sargassum glaucescens. Pharmacognosy Res. **7**, 314–321 (2015).
73. Vinoth Kumar, T. *et al.* Fucoidan - A α-d-glucosidase inhibitor from *Sargassum wightii* with relevance to type 2 diabetes mellitus therapy. Int. J. Biol. Macromol. **72**, 1044–1047 (2015).
74. Motshakeri, M. *et al.* Effects of brown seaweed (*Sargassum polycystum*) extracts on kidney, liver, and pancreas of type 2 diabetic rat model. Evidence-based Complement. Altern. Med. **2014**, (2014).
75. Selvaraj, S., Palanisamy, S. Investigations on the anti-diabetic potential of novel marine seaweed *Sargassum longiotom* against alloxan-induced diabetes mellitus: A pilot study. Bangladesh J. Pharmacol. **9**, 194–197 (2014).
76. Motshakeri, M., Ebrahimi, M., Goh, Y. M., Matanjun, P., Mohamed, S. *Sargassum polycystum* reduces hyperglycaemia, dyslipidaemia and oxidative stress via increasing insulin sensitivity in a rat model of type 2 diabetes. J. Sci. Food Agric. **93**, 1772–1778 (2013).
77. Lee, C.-. W., Han, J.-S. Hypoglycemic effect of *Sargassum ringgoldianum* extract in STZ-induced diabetic mice. Prev. Nutr. Food Sci. **17**, 8–13 (2012).
78. Kim, S.-N., Lee, W., Bae, G.-U., Kim, Y. K. Anti-diabetic and hypolipidemic effects of *Sargassum yezoense* in db/db mice. Biochem. Biophys. Res. Commun. **424**, 675–680 (2012).
79. Hanefeld, M. The Role of Acarbose in the Treatment of Non–Insulin-Dependent Diabetes Mellitus. J. Diabetes Complications. **12**, 228–237 (1998).
80. Kawamura-Konishi, Y. *et al.* Isolation of a new phlorotannin, a potent inhibitor of carbohydrate-hydrolyzing enzymes, from the brown alga *Sargassum patens*. J. Agric. Food Chem. **60**, 5565–5570 (2012).
81. Kim, J. S. Effect of Rhemanniae radix on the hyperglycemic mice induced with streptozotocin. J. Korean Soc. Food Sci. Nutr. (2004).
82. Kwon, M.-J., Nam, T.-J. Porphyran induces apoptosis related signal pathway in AGS gastric cancer cell lines. Life Sci. **79**, 1956–1962 (2006).
83. Min, K.-H., Kim, H.-J., Jeon, Y.-J., Han, J.-S. Ishige okamurae ameliorates hyperglycemia and insulin resistance in C57BL/KsJ-db/db mice. Diabetes Res. Clin. Pract. **93**, 70–76 (2011).
84. Pushpamali, W. A. *et al.* Isolation and purification of an anticoagulant from fermented red seaweed Lomentaria catenata. Carbohydr. Polym. **73**, 274–279 (2008).
85. Watanabe, J., Kawabata, J., Kurihara, H., Niki, R. Isolation and Identification of α-Glucosidase Inhibitors from Tochu-cha (*Eucommia ulmoides*). Biosci. Biotechnol. *Biochem.* **61**, 177–178 (1997).
86. Heo, S.-J., Park, E.-J., Lee, K.-W., Jeon, Y.-J. Antioxidant activities of enzymatic extracts from brown seaweeds. Bioresour. Technol. **96**, 1613–1623 (2005).
87. Kopelman, P. G. Obesity as a medical problem. Nature**. 404**, 635–643 (2000).
88. MacArtain, P., Gill, C. I. R., Brooks, M., Campbell, R., Rowland, I. R. Nutritional Value of Edible Seaweeds. Nutr. Rev. **65**, 535–543 (2007).
89. Nwosu, F. *et al.* Anti-proliferative and potential anti-diabetic effects of phenolic-rich extracts from edible marine algae. Food Chem. **126**, 1006–1012 (2011).
90. Patel, S. Therapeutic importance of sulfated polysaccharides from seaweeds: updating the recent findings. 3 Biotech **2**, 171–185 (2012).
91. Wei, Y., Li, Z., Hu, Y., Xu, Z. Inhibition of mouse liver lipid peroxidation by high molecular weight phlorotannins from *Sargassum kjellmanianum*. J. Appl. Phycol. **15**, 507–511 (2003).
92. Organization, W. H. WHO Global report on diabetes. (2016).
93. Kavishankar, G. B., Lakshmidevi, N. Anti-diabetic effect of a novel N-Trisaccharide isolated from Cucumis prophetarum on streptozotocin–nicotinamide induced type 2 diabetic rats. Phytomedicine. **21**, 624–630 (2014).
94. Moller, D. E. New drug targets for type 2 diabetes and the metabolic syndrome. Nature **414**, 821–827 (2001).
95. Tomkin, G. H. Targets for Intervention in Dyslipidemia in Diabetes. Diabetes Care **31**, S241–S248 (2008).
96. Zhang, J. *et al.* Antidiabetic properties of polysaccharide- and polyphenolic-enriched fractions from the brown seaweed *Ascophyllum nodosum*This article is one of a selection of papers published in this special issue (part 2 of 2) on the Safety and Efficacy of Natural Healt. *Can.* J. Physiol. Pharmacol. **85**, 1116–1123 (2007).
97. Kamei, Y., Tsang, C. K. Sargaquinoic acid promotes neurite outgrowth via protein kinase A and MAP kinases-mediated signaling pathways in PC12D cells. Int. J. Dev. Neurosci. **21**, 255–262 (2003).
98. Lee, S.-H., Jeon, Y.-J. Anti-diabetic effects of brown algae derived phlorotannins, marine polyphenols through diverse mechanisms. Fitoterapia. **86**, 129–136 (2013).
99. Liu, L., Heinrich, M., Myers, S., Dworjanyn, S. A. Towards a better understanding of medicinal uses of the brown seaweed *Sargassum* in Traditional Chinese Medicine: A phytochemical and pharmacological review. J. Ethnopharmacol. **142**, 591–619 (2012).
100. Szkudelski, T. The mechanism of alloxan and streptozotocin action in B cells of the rat pancreas. Physiol. Res. **50**, 537–546 (2001).
101. Gupta, S., Abu-Ghannam, N. Bioactive potential and possible health effects of edible brown seaweeds. Trends Food Sci. Technol. **22**, 315–326 (2011).
102. Kellogg, J., Grace, M. H., Lila, M. A. Phlorotannins from Alaskan seaweed inhibit carbolytic enzyme activity. Mar. Drugs **12**, 5277–5294 (2014).
103. Reddy, P., Urban, S. Meroditerpenoids from the southern Australian marine brown alga *Sargassum*

fallax. Phytochemistry **70**, 250–255 (2009).
104. Ezugwu, A. E. *et al.* Automatic clustering algorithms: a systematic review and bibliometric analysis of relevant literature. Neural Comput. Appl. **33**, 6247–6306 (2021).
105. Shiau, W.-L., Dwivedi, Y. K., Yang, H. S. Co-citation and cluster analyses of extant literature on social networks. Int. J. Inf. Manage. **37**, 390–399 (2017).
106. Cheng, K.-H., Tang, K.-Y., Tsai, C.-C. The mainstream and extension of contemporary virtual reality education research: Insights from a co-citation network analysis (2015–2020). Educ. Technol. Res. Dev. **70**, 169–184 (2022).
107. Grames, E. M., Stillman, A. N., Tingley, M. W., Elphick, C. S. An automated approach to identifying search terms for systematic reviews using keyword co-occurrence networks. Methods Ecol. Evol. **10**, 1645–1654 (2019).