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The visualized knowledge map and hot topic analysis of glomalin-related soil proteins in the carbon field based on Citespace

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Abstract

Arbuscular mycorrhizal fungi (AMF) in the soil have many positive effects on growth, nutrient acquisition, and stress tolerance of host plants, as well as soil fertility, soil structure, and soil ecology. Glomalin-related soil proteins (GRSP) are a mixture of humic substances and heat-stable glycoproteins, primarily of AMF origin. GRSP are as an important component of soil organic carbon (C) pools, which can stabilize and sequestrate C, thus reducing soil C emissions for slowing down global warming. Based on the CiteSpace software and the core collection of Web of Science as the database, this study made a visual analysis of GRSP's literature in the C field published from 1999 to 2022, including the number of publications, countries, institutions, co-cited literature, keywords, top cited papers, etc. The study regarding the GRSP in the C field could be divided into the initial stage (1999–2009), the steady stage (2010–2018), and the explosive stage (2019–2022). The Chinese Academy of Sciences is the organization with the most publications, and the United States, China, and India are the three leading nations in the C field of GRSP. However, there was little collaboration among the participating countries and the study's institutions. The focus of the research has shifted from the composition and content of GRSP in C to the question of whether C in GRSP affects soil properties. Future research was also prospected.

Keywords Aggregate stability, Carbon sequestration, Glomalin, Mycorrhiza, Soil aggregate, Soil organic carbon

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Introduction

Arbuscular mycorrhizal fungi (AMF) are an important group of soil microorganisms that can form symbiotic associations with the roots of more than 80% of terrestrial plants [1]. AMF can enhance the host plant's ability to absorb water and mineral nutrients, thus promoting plant growth [2]. Additionally, the mycorrhizal symbiosis also enhances plants' ability to withstand stress and has a positive impact on improving soil structure and maintaining soil health [3, 4]. AMF also produce an insoluble and heat-resistant recalcitrant glycoprotein, glomalin (Fig. 1) [5], which can exhibit an immunofluorescent reaction with the monoclonal antibody Mab32B11 [6]. Generally, purified glomalin typically contains the following elements: carbon (C), hydrogen (H), oxygen (O), nitrogen (N), phosphorus (P), potassium (K), calcium (Ca), magnesium (Mg), copper (Cu), iron (Fe), and so on [7]. Glomalin also contains additional nonglomalin components, hence Rillig [8] proposed that the term "glomalin-related soil proteins" (GRSP) should be used in its place.

Numerous studies into the structure, distribution, and function of GRSP have been carried out since they were first named. Structurally, the mass spectrometry analysis revealed that GRSP are an N-chain glycoprotein with part of amino acid sequence showing the homology to heat shock protein 60 (Hsp60) sequence. It is evident from a substantial body of literature that GRSP contain 2-4% N, 35-40% C, 4-6% H, 33-49% O, 0.8-8.8% Fe, 1.2-2.7% K, 0.3-0.7% Ca, 0.03-0.3% P, 3.0-9.7% Si, 2.8-3.4% Na, 0.3-0.5% Mg, 1.3-4.8% Al, 0.035-0.153% Mo, 0.011-0.018% Zn, 0.014-0.025% Cu, and 0.020-0.037% Mn [7, 9–12]. In terms of the distribution, GRSP can be detected in most ecosystems, including agricultural fields (0.32-0.71 mg/g), forests (1.1 mg/g), deserts (0.003-0.13 mg/g, temperate forests (0.6–5.8 mg/g), temperate grasslands (0.23-2.5 mg/g), and tropical rainforests (2.6-13.5 mg/g), respectively [11]. In terms of their functions, GRSP can promote the formation of soil aggregates, maintain the stability of soil aggregates, and improve soil structure (Fig. 1) [13–15]. In addition, GRSP has a turnover time of 8.4-61.3 years and a high soil accumulation capacity, both of which can promote soil carbon (C) storage [16, 17]. Because GRSP can bind, sequester, stabilize, and reduce the availability of heavy metals, they are able to lessen the toxicity of heavy metals to plants [8, 17–19]. Under adverse environmental conditions, AMF can produce more GRSP as a stress-inducible protein to improve plant stress resistance [20, 21]. Another important function of GRSP is C fixation and recycling [22], which reduces soil CO₂ emissions and increases the average residence time of C in the soil (or other stabilizing pools),



Fig. 1 The release of GRSP by arbuscular mycorrhizal fungi and its development stage in the C field and associated countries and institutions in the publications of GRSP in the C field

paving the way for C stabilization [23–26]. GRSP can contribute about 27% of soil organic carbon (SOC), while soil humus only contributes about 8% of C, resulting in 2-24 times higher C contribution capacity of GRSP than that of soil humus [27]. The contribution of GRSP to the total soil C content is higher than that of soil organic C [28]. This is due to the fact that GRSP have a low soil turnover rate and a large capacity for accumulation [29].

There is also excellent literature on GRSP [12, 21, 29-31], but they are characterized primarily by traditional qualitative descriptions and rarely use quantitative methods to generalize and summarize. Traditional literature analysis methods cover a large body of information that can be creatively and efficiently presented through figures and tables, while they have obvious limitations such as limited literature, a high rate of literature omission, and repeatability. In comparison to traditional qualitative methods, quantitative literature analysis can assist researchers in quickly sorting out specific information. It can be used to analyze the characteristics and hot topics of a particular field, as well as to estimate the impact of the research field and identify emerging trends [32]. Among bibliometric analysis tools, CiteSpace (https:// citespace.podia.com/) is the most widely used bibliometric analysis tool due to its features: (i) simple operation, multiple functions, clear and comprehensive visualization [33]; (ii) visualization of the structure, rule and distribution of scientific knowledge [33]; and (iii) obtaining the map of scientific knowledge to clarify the analysis of the hot topic of the research field [34]. As a result, CiteSpace has been used for the bibliometric analysis of rhizospheric microorganisms [35], phytoremediation [36], antibiotics in soil [37], cleaner production [38], and other topics. Only a few studies have used the CiteSpace to evaluate AMF. For example, Xu et al. [39] used the CiteSpace to analyze the advance of legume mycorrhizal research. Wang et al. [40] used the CiteSpace to analyze the state of AMF over the past 30 years. In this study, we used the CiteSpace software in conjunction with bibliometric methods to conduct a visual analysis of GRSP literature on the Web of Science (https://www.webofscien ce.com/wos) (WOS) in the C field. We discussed the countries, institutions, cited literature, and keywords, and comprehensively summarized the research advance, hot topics and future direction of GRSP in the C field, to bring clarity for the research of GRSP and C.

Materials and methods

Data sources

The data in this study were obtained from the WOS core collection database using the keywords "GRSP", "glomalin-related soil protein", or "glomalin" and "carbon", respectively. Since glomalin was only discovered in 1996, the search period was set from January 1, 1996 to December 31, 2022, and 484 papers were exported after removing literature such as conference reports and book descriptions that were not related to the topic.

Data analysis

Using the CiteSpace v.6.1.R6(64-bit) software, the time slice was one year. The node types were Country, Institution, Keyword, Reference, etc. with the node intensity set to Cosine to generate the statistical data and a visual cooccurrence of the GRSP and C research field. In CiteSpace, node types such as Institution, Country, Keyword, and Reference were chosen for the visualization. In addition, Microsoft Excel 2019 was used to perform a preliminary statistical analysis on the data of 458 literatures retrieved, including the annual number of publications, countries of publication, and keywords. The OriginPro 2021 was utilized to draw figures. In co-occurrence cluster analysis networks, nodes represented specific Country, Institution or Keyword, the size of nodes represented their productivity, and the thickness of lines between nodes represented collaborative relationships [32].

Results

Changes in the number of papers published every year

The number of papers published each year can reflect the research's dynamic change. The papers related to GRSP and C around the world from 1996 to 2022 are shown in Fig. 2. Since the initial paper by Rillig et al. in 1999 [41] was published, the number of papers associated with GRSP and C has gradually increased each year. Particular in 2019, the number of papers published increased by 100%, compared to 2018, and the number of papers published for the first time exceeded 45. The research related to GRSP and C could be divided into three stages: (i) the initial stage (1999–2009), in which the number of relevant papers from the initial to maintenance to

less than 10 papers; (ii) the steady stage (2010 - 2018), in which the number of papers exceeded 10 and was close to 30, accompanied by a steady development trend; (iii) the explosive stage (2019 - 2022), in which the number of papers increased explosively, from 48 in 2019 to 68 in 2021, and maintained at more than 60 in 2022, indicating that the research on GRSP and C has been paid more and more attention in recent years. The linear regression analysis also revealed a positive correlation between the year of publication and the number of published papers, indicating an increasing interest in the field.

Changes in the countries of published papers

Changes in the countries of published papers can reflect a country/region's attention to research in a certain field. By analyzing the country publishing papers from the WOS, a visualization map was created (Fig. 3). Data from 60 countries were analyzed. A total of 60 nodes and 154 lines appeared. The information of the top 10 countries with the number of published papers was selected and summarized into Table 1. China, USA, and India have more studies related to GRSP in C than any other country, with China leading the list with 181 papers, accounting for 39.52% of the total number of papers in the WOS database; USA is the first country to report the work regarding GRSP and C, with 96 papers starting in 1999; India has 71 papers. China had the highest centrality (an indicator reflecting the importance of nodes in the network), ranking first with 0.54 (Table 1). Spain and France ranked fifth and ninth with only 32 and 16 papers, respectively, but they also ranked second and third with 0.33 and 0.32 centrality, respectively. USA, on the other



Fig. 2 Number of papers per year in the C field of GRSP in WOS

Year



Fig. 3 Changes in the country of published papers. Here, each circle represented a country, the size of the circle represented the number of published papers, and the lines represented co-citation. The outer purple circle represented the centrality of the intermediary

Table 1 Characteristics and frequency of national papers rankedin the top 10 countries

Country	Frequency	Centrality	Starting year	
China	181	0.54	2003	
USA	96	0.27	1999	
India	71	0.08	2009	
Brazil	47	0.09	2006	
Spain	32	0.33	2003	
Australia	27	0.10	2002	
Czech Republic	23	0.06	2016	
Germany	19	0.26	2007	
France	16	0.32	2007	
Chile	13	0.03	2000	

hand, ranked fourth with a centrality of 0.27. In summary, China, Spain, France and USA had high centrality and collaboration (based on the Citespace algorithm, the thickness and density of connections between different nodes represent the degree of collaboration) in the research related to GRSP and C.

Changes in institutional papers

The institutional co-occurrence mapping of internationally published papers regarding GRSP and C was shown in Fig. 4. The Chinese Academy of Sciences is the most frequently appearing institution, with 62 papers occurrences, far more than other institutions (Table 2). The Chinese Academy of Sciences had a purple outer circle outside the node, with a centrality of 0.26, ranking first (Fig. 4), indicating its high intermediary centrality, frequent collaboration, and close connection with other countries. The second most frequent institution was Yangtze University, with 25 papers occurrences. The third frequent institution was the University of Chinese Academy Sciences with 24 papers appearances. Among the top eight institutions, China had the largest number of institutions, accounting for 50% of the total, demonstrating that China is the country with the largest number of international literature contributions. The University of Montana with 16 papers, had a centrality of 0.25, second only to the Chinese Academy of Sciences. The network density of the map was 0.0071, indicating that the collaboration was low at the institutions.

Changes in literature co-citation

The literature co-citation (two or more papers that are simultaneously cited by one or more subsequent papers are said to constitute a co-citation relationship) network mapping (Fig. 5) showed 879 nodes with 3572 links and a network density of 0.0093, where the article of Singh et al. [22] in 2017 from India entitled "Contribution of glomalin to dissolve organic carbon under different land uses and seasonality in dry tropics" was cited the highest 42 times. The study conducted by Singh et al. [22] revealed the role of GRSP in enhancing soil health and SOC sequestration in arid tropical agro-ecosystems. The second most cited literature was still Singh et al. [42] entitled "Effect of long term land



Fig. 4 Changes in institutions of published papers

Table 2 Characteristics and frequency of institutional papersranked in the top 8 institutions

Institution	Frenquency	Centrality	Starting year
Chinese Acad Sci	62	0.26	2003
Yangtze Univ	25	0.15	2012
Univ Chinese Acad Sci	24	0.05	2013
USDA ARS	16	0.02	2000
Univ Montana	16	0.25	2000
Xiamen Univ	14	0.01	2018
Univ Western Australia	10	0.09	2015
Northwest A&F Univ	10	0.04	2016

use systems on fractions of glomalin and soil organic carbon in the Indo-Gangetic plain". They reported that the factors involved in SOC formation contributed to GRSP production by promoting the proliferation of AMF, coupled with a high contribution of C in GRSP to non-particulate organic C for stabilizing SOC.

Based on the centrality of the cited literature, Wu et al. [43] from China in 2012 had the highest centrality among the 20 articles with more than 20 citations (Table 3), in which they reported the spatial distribution of GRSP in citrus rhizosphere and its correlation with root and soil carbohydrates. The second-ranked centrality literature was also from Wu et al. [44] in 2015, where the difficultly extractable glomalin-related soil protein (DE-GRSP) concept was proposed and AMF-mediated GRSP production was not dependent on substrate P levels. The review by Rillig [8] in 2004 with the third-ranked centrality proposed the term GRSP, instead of glomalin. In summary, the three papers constitute the major supporting literature in GRSP and C research due to their high centrality and high citations.

Changes in research hot topics

Research hot topics refer to the issues and topics that are discussed by a relatively large number of scholars within a certain period of time. Keywords are typically used to summarize the core content of an article, reflecting the article's value and direction. A total of 458 articles were analyzed by Citespace, and the research hotspot map was drawn by selecting "Keywords" in NodeType, as shown in Fig. 6, in which there were 511 network nodes and 3598 connections. The keywords were represented by nodes. The more times the keywords appear, along with larger nodes, which means the more scholars pay attention to it, indicating that it is the hotspot and trend of research. The most frequent keyword was "arbuscular mycorrhizal fungi" (Fig. 6), which appeared 225 times (Table 4), because GRSP originates from the spores and hyphae of AMF. The following keywords were "aggregate stability", "carbon", "nitrogen", "organic matter", and "organic matter", all of which appeared more than 100 times (Table 4). This indicated that GRSP research in recent years has



Fig. 5 Changes in literature co-citation

mostly focused on the stability of soil aggregates and their potential for C sequestration. The subsequent keywords "diversity", "enzyme activity", "growth", and "land use" revealed that the influence of GRSP on land management is relatively important. The keywords "aggregate stability" and "organic matter" had the highest centrality, because GRSP functioning indicates that soil aggregate stability and soil organic matter have always been the hot topics in the GRSP research.

Changes in citation burst terms

CiteSpace can extract the citation burst terms (the words with a large change in frequency within a short period of time) from a large number of literature subject terms, so as to clearly show the research fronts in the field. Based on the citation burst term analysis, the top 13 keywords were obtained in the fields of GRSP and C after 1999 (Fig. 7), of which "carbon dioxide" had the highest citation burst term lasting 13 years, followed by "hyphae" lasting 12 years. Initially, "carbon dioxide" was a hot topic during 1999–2012, followed by "soil carbon" (2003–2006) and "carbon" (2013–2015). "Soil properties" and "quality" have emerged a new hot spot, indicating that the beneficial effect of GRSP on soil properties and quality has attracted attention in recent years.

Discussion

Studies have revealed the potential role of GRSP in the soil C sequestration [16, 45]. GRSP in the C field has gained increasing attention. A total of 484 papers

cantered on GRSP in the C field were collected for this study, which was conducted by more than 500 scholars from 360 research institutions in 60 countries.

There are many countries conducting research on GRSP in the C field, including the United States, China, India, Brazil, Spain, Australia, etc. Such work is primarily focused on China, the United States and India, with less involvement from other countries. The United States was the earliest country to start the research, discovered the existence of GRSP, and developed extracted and quantified methods [5, 6, 8]. China started the research later than the other countries, but it currently has published the most publications. These publications covered in wetlands [17], plateaus [46, 47], sandy areas [48], black soil [49], and coastal areas [50]. Among the research institutions, the Chinese Academy of Sciences is by far the most published institution. In India, agricultural management [51] and biochar [52] were evaluated with an emphasis on agricultural soils. In the future, collaboration between countries and institutions needs to be strengthened to promote the research of GRSP in the C field. In recent years, research on GRSP and C has ranged from CO_2 at the beginning to soil characteristics now. It can be seen that, the contents and components of GRSP in C were determined when GRSP-related studies first started, and following studies mostly focused on whether GRSP in C contributed to soil characteristics. As a result, the research involving GRSP in the C field includes C sequestration, C stability, soil aggregate stability, and other soil characteristics [12, 53].

Table 3 Top 20 co-cited papers in the field

Authors	Frequency	Centrality	Published year	Title
Singh et al.	42	0.05	2017	Contribution of glomalin to dissolve organic carbon under different land uses and seasonality in dry tropics
Singh et al.	37	0.02	2016	Effect of long term land use systems on fractions of glomalin and soil organic carbon in the Indo-Gangetic plain
Wang et al.	32	0.01	2017	Glomalin contributed more to carbon, nutrients in deeper soils, and differently associ- ated with climates and soil properties in vertical profiles
Zhang et al.	32	0.01	2017	Recalcitrant carbon components in glomalin-related soil protein facilitate soil organic carbon preservation in tropical forests
Kumar et al.	30	0.04	2018	Distribution of soil organic carbon and glomalin related soil protein in reclaimed coal mine-land chronosequence under tropical condition
Wang et al.	26	0.02	2018	Spatial distribution of glomalin-related soil protein and its relationship with sediment carbon sequestration across a mangrove forest
Fokom et al.	25	0.04	2012	Glomalin related soil protein, carbon, nitrogen and soil aggregate stability as affected by land use variation in the humid forest zone of south Cameroon
Wu et al.	23	0.17	2012	Spatial distribution of glomalin-related soil protein and its relationships with root mycorrhization, soil aggregates, carbohydrates, activity of protease and β -glucosidase in the rhizosphere of Citrus unshiu
Rillig	22	0.12	2004	Arbuscular mycorrhizae, glomalin, and soil aggregation
Vasconcellos et al.	22	0.07	2016	Arbuscular mycorrhizal fungi and glomalin-related soil protein as potential indicators of soil quality in a recuperation gradient of the Atlantic forest in Brazil
Wu et al.	22	0.14	2015	Arbuscular mycorrhiza mediates glomalin-related soil protein production and soil enzyme activities in the rhizosphere of trifoliate orange grown under different P levels
Zhang et al.	22	0.03	2015	Glomalin-related soil protein responses to elevated CO_2 and nitrogen addition in a subtropical forest: Potential consequences for soil carbon accumulation
Zhang et al.	22	0.05	2017	Effects of soil salinity on the content, composition, and ion binding capacity of glomalin-related soil protein (GRSP)
Holatko et al.	21	0.01	2021	Glomalin–Truths, myths, and the future of this elusive soil glycoprotein
Rosier et al.	21	0.02	2006	Glomalin-related soil protein: assessment of current detection and quantification tools
Steinberg et al.	21	0.02	2003	Differential decomposition of arbuscular mycorrhizal fungal hyphae and glomalin
Koide et al.	20	0.08	2013	Behavior of Bradford-reactive substances is consistent with predictions for glomalin
Liu et al.	20	0.05	2020	Glomalin-related soil protein affects soil aggregation and recovery of soil nutrient fol- lowing natural revegetation on the Loess Plateau
Rillig et al.	20	0.04	2003	Glomalin, an arbuscular-mycorrhizal fungal soil protein, responds to land-use change
Wu et al.	20	0.03	2014	Direct and indirect effects of glomalin, mycorrhizal hyphae, and roots on aggregate stability in rhizosphere of trifoliate orange

According to the number of published papers in each year, we divided GRSP research in the C field into three stages, namely, the initial stage between 1999 and 2009 (<10 papers/year), the steady stage between 2010 and 2018 (10-30 papers/year), and the explosive stage between 2019 and 2022 (>48 papers/year). Among them, the steady stage focused on the impact of different land uses on GRSP and C content [54], as well as distribution patterns, C cycling, and plant growth of GRSP in various ecosystems [55-58]. In the explosive stage, the number of annual papers increased significantly, and scholars paid more attention to the function of GRSP in the C cycle [59], as well as the contribution of GRSP and biochar to improving microbial community conditions in heavy metal-contaminated soil [60].

In general, the high centrality of literature indicates that the literature is a key hub connecting two distinct fields [61]. When the centrality of a node is ≥ 0.1 , it is called a critical node. As a result, if a node has a high centrality, it has a high scientific influence [62]. In this study, GRSP research in recent years has primarily focuses on the stability of soil aggregates and their C sequestration. GRSP can bind organics, clays, minerals, oxides, and microorganisms [43, 63-65]. In addition, GRSP contain 85% polysaccharides that are resistant to microbial degradation for an extended period of time [66]. AMF, the producer of GRSP, can combine microaggregates into macroaggregates [23, 26, 67-69]. Hence, AMF stabilize soil aggregates to increase the residence time of organic C in soil. Subsequently, GRSP can form a protective layer on macroaggregates with the help of its hydrophobicity [70], resulting in the increase in the C sequestration in soil aggregates.



Fig. 6 Changes in research hot topics

 Table 4
 Characteristics and frequency of research hot topics

Keywords	Frequency	Centrality	
Arbuscular mycorrhizal fungi	225	0.07	
Glomalin	191	0.07	
Aggregate stability	164	0.11	
Carbon	154	0.06	
Nitrogen	117	0.09	
Organic matter	107	0.11	
Protein	94	0.06	
Hyphae	90	0.06	
Organic carbon	72	0.03	
Glomalin-related soil protein	64	0.12	
Diversity	60	0.07	
Stability	51	0.03	

The role of GRSP in soil properties and quality has been gaining popularity. Such results were reported in forests [71, 72], farmland [73], grasslands [74, 75], Wetlands [76, 77], and plateau [78]. Land use is an important factor affecting SOC concentrations, with tillage methods and land management being the most critical factors influencing soil GRSP levels [51, 79, 80]. Several climatic, biological and soil factors affect the production of GRSP by AMF [21]. Soil GRSP levels are regulated by a balance between AMF production and microbial decomposition, dependent on AMF assimilates from host plants [81]. Studies have revealed a significantly positive correlation between GRSP levels and SOC concentrations [22, 82], because GRSP contain organic C [83]. Therefore, different land use patterns and climate conditions will lead to dynamic changes in C [84]. Utilizing data models can help in-depth understanding of changes in the C of GRSP. The establishment of a global database of GRSP and organic C is critical to understanding the contribution of GRSP to SOC and the impact of global warming.

Conclusions and prospect

This study revealed the characteristics of GRSP in the C field by means of bibliometric analysis. The research of GRSP in the C field is divided into three stages, namely the initial stage (1999–2009), the steady stage (2010–2018), and the explosive stage (2019–2022), with a variety of hot topics. Over the past three years, more than 60 papers have reported the finding of GRSP in the C field, and many countries have also participated in the research field, indicating that GRSP in the C field has emerged as an important hot spot with promising future prospects. However, there are the following research gaps that need to be addressed:

- (i) The underlying mechanism and influencing factors of how GRSP stabilize and sequestrate C remain unclear, dependent on deep collaboration between countries and institutions.
- (ii) There is the lack of quantitative research revealing the role of GRSP in alleviating greenhouse effects.
- (iii) How to effectively use both GRSP and AMF to improve soil structure and increase crop yield.

Top 13 Keywords with the Strongest Citation Bursts

Keywords	Year	Strength	Begin	End	1999 - 2022
carbon dioxide	1999	4.84	1999	2012	
hyphae	2000	7.15	2003	2015	
soil carbon	2003	3.73	2003	2006	
soil organic matter	2007	3.56	2007	2008	
land use	2005	3.79	2011	2017	
plant	2008	3.24	2011	2014	
quantification	2008	3.83	2012	2015	
carbon	2000	5.11	2013	2015	
fungi	2000	5.01	2013	2016	
inoculation	2013	3.62	2013	2015	
rhizosphere	2014	5.2	2015	2017	
soil property	2020	3.82	2020	2022	
quality	2014	3.57	2020	2022	

Fig. 7 The order of top 13 citation burst terms based on the starting year

- (iv) How to purify GRSP is crucial for understanding its structure and function (especially the role of C field). Accurate quantification of GRSP will be of great help to evaluate the contribution of GRSP to C sequestration.
- (v) Plants, soils, environmental conditions, and AMF should be brought together to explore how to effectively increase GRSP concentrations and study it in the C field.

Acknowledgements

We are sincerely grateful to the two anonymous reviewers for their constructive comments and language recommendations on this article. The authors would like to extend their sincere appreciation to the Researchers Supporting Project Number (RSP2023R356), King Saud University, Riyadh, Saudi Arabia.

Author contributions

CD, YNZ and QSW conducted the experiment. CD wrote the original manuscript. CD prepared figures. All authors reviewed and edited the manuscript.

Funding

This work was supported by the National Natural Science Foundation of China (32272643). The authors would like to extend their sincere appreciation to the Researchers Supporting Project Number (RSP2023R356), King Saud University, Riyadh, Saudi Arabia.

Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication Not applicable.

Competing interests

The authors declare no competing interest regarding the publication of this work.

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Received: 9 March 2023 Accepted: 6 June 2023 Published online: 13 June 2023

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