



Bibliometric analysis of research on microcystins in China and worldwide from 1991 to 2011

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ABSTRACT

Blue green algae cyanobacterial blooms can produce a family of toxins, microcystins, *Microcystis aeruginosa*. These proliferate in warm water bodies where nutrients are available, thus drinking water can be contaminated. This study evaluates the scientific output of microcystin research in China relative to that worldwide during 1991–2011 and explores future research directions. Data were retrieved from the online version of Web of Science from 1991 to 2011. Articles referring to microcystins were evaluated by yearly number of publications, cumulative number of articles, distribution of source countries, institutes, subject categories, journals, as well as by author keywords in these years based on the predictive *h*-index. It appeared that the quantity of articles published by Chinese researchers had increased at a quicker pace than the worldwide average rate since 2001. Article visibility was not in proportion to its article numbers. Moreover, China showed a different focus and future direction on microcystin research than other countries.

Keywords: Drinking water; Microcystins; Hepatotoxicity; Cyanobacterial blooms; Web of Science; Research trends

1. Introduction

Enhancement of eutrophication has affected increasing numbers of freshwater bodies not only in China but also in many other countries [1]. One of the most serious consequences is the frequent occurrence of harmful cyanobacterial blooms, which have made available good quality freshwater more sparse [2]. These blooms usually occur suddenly in warmer seasons and cover water surface rapidly, resulting in the

death of aquatic animals due to hypoxia or the toxins of these blooms [3]. In addition, the smell of the blooms is disgusting in summer. What is worse is that cyanobacteria produce large amounts of secondary metabolites named cyanotoxins. These substances are responsible for the death of fish, birds, wild animals and livestock. In many countries where toxic cyanobacterial blooms occur in freshwater, harmful effects of the toxins on human beings have been reported [4,5].

So far, many cyanotoxins have been isolated and identified. Among them, microcystins are the best

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studied. These are cyclic heptapeptides, produced mainly by *Microcystis aeruginosa*, but also by other *Microcystis* species and other genera, such as *Anabaena*, *Oscillatoria*, and *Haphalosiphon* [6]. More than 80 kinds of microcystins have been identified; these share a general structure of cyclo (-D-Ala-X-D-MeAsp-Z-Adda-D-Glu-Mdha), X and Z being the variable L-amino acids [7]. One of the most common and toxic microcystins is the Microcystin-LR (MC-LR), characterized by the presence of leucine (L) and arginine (R) in various positions [8]. Other variants that also occur frequently are MC-RR and MC-YR [9].

Microcystins are well known for their hepatotoxicity not only due to their ability to cause acute poisonings but due to their tumor promotion potentials caused by chronic exposure of people to low concentration of microcystins in drinking water. The toxic mechanism is that they have a great ability to inhibit the protein phosphorylation process of serine/threonine-specific protein phosphatases, PP1 and PP2A, by binding to the catalytic subunits of these enzymes [10–12]. The consequence of the inhibition is disastrous; the hyperphosphorylation of the cytoskeleton proteins leads to the alteration of cell shapes, the loss of cell adhesion at desmosomes and the destruction of hepatocytes [6]. In addition, the inhibition of phosphorylation process is also related to tumor promotion in that PP2A was showed to have an ability to suppress the development of tumor cells [13]. There also have been reports that microcystins can evoke the production of reactive oxygen species (ROS) and cause DNA damage in mammalian cells [14,15].

In China, many lakes, reservoirs and recreational waters are in the state of heavy eutrophication [16–21]. With the frequency of occurrence of toxic cyanobacterial blooms, the hazard of microcystins has been recognized by the public. In late May, 2007, the 2 million people living in the watershed of Lake Tai, the third largest freshwater lake in China, suffered from a drinking water crisis for at least a week caused by a massive bloom of the toxin producing cyanobacteria, *Microcystis* spp. [22]. It was also reported that the incidence of primary liver cancer in eastern region of China was related to the presence of microcystins in drinking water [23,24].

China has started paying attention to microcystins and taking steps towards them. Studies about them have been published by researchers not only from China but also from many other countries. However, algal blooms are still not sufficiently controlled, and microcystins in drinking water remain a huge public problem. So, information about this should be collected for the future research to reduce or prevent the hazard of the microcystins, and for establishing

uniform water quality to ensure the safety of the water. These will be very helpful for people in those regimens who drink water straightly from the surface of the river or the pond. This study aims to bibliometrically analyze all the literatures related to microcystins published from 1991 to 2011 in China and in worldwide, so as to find out the characteristics of these literatures and identify patterns, tendencies, or hot-spots existed in them. Furthermore, this will provide a comprehensive evaluation of current status of research in China relative to that in worldwide. Such information may be helpful for those who are responsible for policy-making and resource allocation and for researchers to establish future research directions.

In this study, a traditional bibliometric method, analysis of yearly article output, cumulative number of articles, languages, source countries, institutes, and journals were used to describe the latest advances in microcystin research in China and in worldwide. Additionally, the newly developed author keywords analysis during different periods was also applied to indicate the directions that the research was taking in China and in worldwide [25,26].

2. Data sources and methodology

Data in these studies of worldwide publications from 1991 to 2011 were retrieved from the online version of the Science Citation Index (SCI), Web of Science, including the SCI-Expanded and the Social SCI databases.

For data collection, the online Web of Science was searched with the "TS=microcystin*" in the advanced search field to compile a bibliography of all papers whose topics were related to microcystin*, which comprises "microcystin," "microcystins," and "microcystin-." A total of 3,062 worldwide publications met the selection criteria including all languages and all document types during the period from 1991 to 2011 worldwide. These publications were categorized as follows:

Articles	2,824	92.2%
Proceedings papers	201	6.6%
Reviews	112	3.7%
Meeting abstracts	82	2.7%
Notes	23	0.8%
Corrections	8	0.3%
Editorial materials	6	0.2%
Letters	4	0.1%
Correction additions	3	0.1%
Book chapters	2	0.1%

Of the 3,062 papers, 412 were published by Chinese researchers, containing 4 document types:

Articles	400	97.1%
Proceedings papers	12	2.9%
Meeting abstracts	6	1.5%
Reviews	6	1.5%

Since journal articles represented the overwhelming majority of peer-reviewed document types within this field, 400 China articles and 2,824 world articles were further analyzed in the following study, while all others were discarded.

For data analysis, information downloaded included all the records and cited literatures, such as names of authors, contact addresses, titles, year of publications, author keywords, times cited, subject categories of the articles, names of journals publishing the articles, and publishers information. These data were saved as txt and analyzed by bibliometric software BibExcel [27] and Microsoft Office Excel. Articles originating from England, Scotland, North Ireland, and Wales were reclassified as being from the UK. The impact factor (IF) of each journal was obtained from the 2011 Journal Citation Reports. It shows the average number of citations to publications published in the two previous years, and is frequently used to assess the relative importance of a journal within its field. To assess the contribution of a country or an institute or a scientist, the *h*-index was applied. It is defined as the number of papers with citation number greater than or equal to *h*, representing not only the actual productivity but also the apparent impact of the published work of a group or a scholar [28]. It has been indicated that the *h*-index has a more superior predictive power than the total number of papers published, the total number of citations garnered, and the average number of citations per paper [29].

3. Results

3.1. Publication distribution of year, cumulative number of articles, and publication languages

The microcystin research developed expeditiously worldwide over the last century, from 1 article in 1904 to 281 articles in 2011. China also showed the same developing trend, from 1 article in 1991 to 98 articles in 2011. The distribution of annual publication output in China and worldwide from 1991 to 2011 is presented in Fig. 1. The worldwide article output showed a steady increase over the past 21 years, whereas the China output increased very slowly from

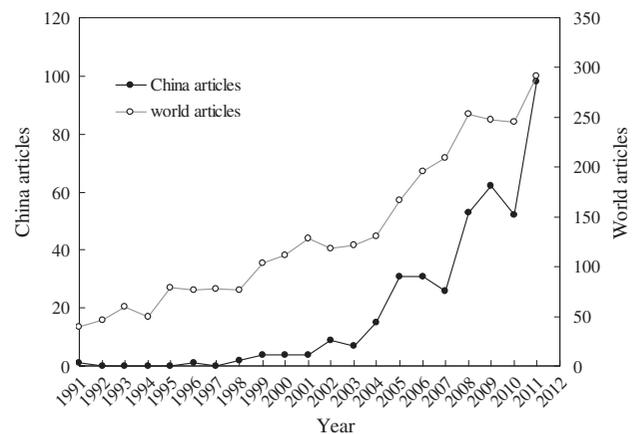


Fig. 1. Number of microcystin articles published by China and worldwide, 1991–2011.

1991 to 2001 but rapidly from 2001 to 2011. It is obvious that the growth rate of China after 2001 (11-fold) is higher than that of the worldwide (2.3-fold).

The progression in the cumulative number of articles in China and worldwide from 1991 to 2011 is also shown in Fig. 2. For China microcystin research, the cumulative number of articles increased very slowly from 1991 to 1999, smoothly from 1999 to 2006, and explosively from 2006 to 2011. An exponential model fits the data very well with a high coefficient of determination ($R^2 = 0.978$). This exponential fitting curve is found to be: $P = 0.3333e^{0.3469y}$ where P is the cumulative number of publications, and y is the number of years since 1991. The worldwide cumulative number of articles showed two different models: power model for 1991–2004 and linear model for 2004–2011. The relationship between the cumulative number of publications (P) and the number of years since 1991 (y) are found to be: $P = 34.502y^{1.3183}$ ($R^2 = 0.996$) and $P = 230.88y - 2084.4$ ($R^2 = 0.994$), respectively.

For worldwide microcystin research, 97.8% articles from 1991 to 2011 were published in English, followed by Chinese (0.58%), Portuguese (0.18%), German (0.14%), Japanese (0.14%), Polish (0.14%), French (0.04%), and Spanish (0.04%). For China research, two languages were used for all SCI publications: English (96%) and Chinese (4%).

3.2. Publication distribution of countries or territories and institutes

Totally, 80 countries or territories have participated in the microcystin research. The top 20 countries with their article output and international collaboration are shown in Table 1. Of these productive countries, 13 are from Europe, 3 from America, 3 from Asia, and 1

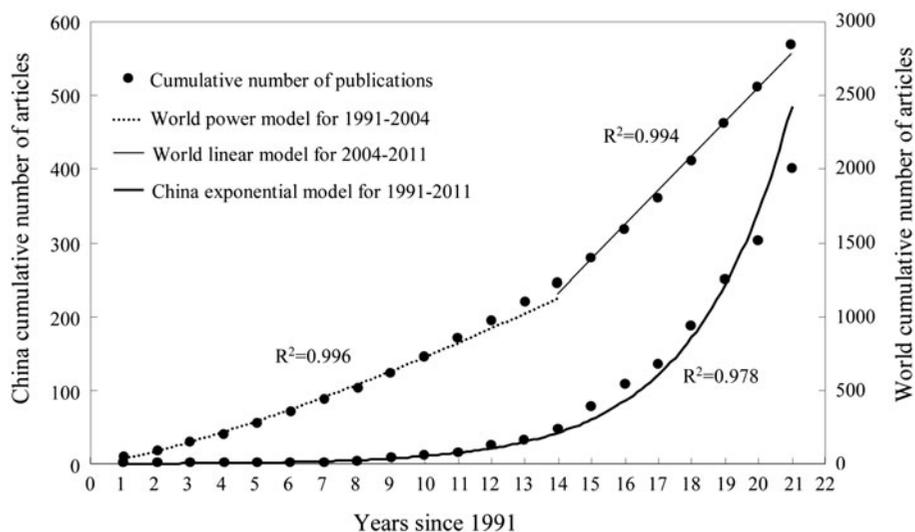


Fig. 2. Cumulative number of microcystin articles published by China and worldwide, 1991–2011.

Table 1
Top 20 most productive countries with article output and international collaboration, 1991–2011

Country	Article output		International collaboration		
	Articles (percentage of all articles)	<i>h</i> -index (rank)	Articles (percentage of articles from country)	Rank of articles	<i>h</i> -index (rank)
The USA (Americas)	590 (20.9)	71 (1)	193 (32.7)	1	47 (1)
China (Asian)	400 (14.2)	31 (7)	63 (15.8)	9	18 (9)
Germany (Europe)	299 (10.6)	54 (2)	170 (56.9)	2	42 (2)
Japan (Asian)	236 (8.4)	44 (4)	83 (35.2)	5	31 (5)
The UK (Europe)	203 (7.2)	50 (3)	98 (48.3)	4	33 (4)
Australia (Oceania)	181 (6.4)	44 (4)	80 (44.2)	6	30 (6)
Finland (Europe)	173 (6.1)	41 (5)	105 (60.7)	3	36 (3)
Canada (America)	147 (5.2)	37 (6)	58 (39.5)	10	22 (7)
France (Europe)	140 (5)	30 (8)	64 (45.7)	8	20 (8)
Brazil (America)	120 (4.2)	22 (10)	42 (35)	11	16 (10)
Spain (Europe)	108 (3.8)	23 (9)	38 (35.2)	12	15 (11)
Poland (Europe)	94 (3.3)	17 (15)	29 (30.9)	14	14 (12)
Portugal (Europe)	83 (2.9)	20 (12)	44 (53.0)	7	16 (10)
South Korea (Asian)	71 (2.5)	16 (16)	23 (32.4)	16	12 (13)
Czech Republic (Europe)	69 (2.4)	15 (17)	18 (26.1)	19	7 (16)
Norway (Europe)	58 (2.1)	21 (11)	31 (53.4)	13	15 (11)
Sweden (Europe)	50 (1.8)	18 (14)	38 (76)	12	18 (9)
Switzerland (Europe)	46 (1.6)	20 (12)	27 (58.7)	15	15 (11)
Netherlands (Europe)	38 (1.3)	19 (13)	20 (52.6)	18	10 (15)
Austria (Europe)	31 (1.1)	15 (17)	21 (67.7)	17	11 (14)

from Oceania. Based on the absolute number of articles, the USA ranked first, with China and Germany coming second and third close behind. The article outputs of the three countries accounted for almost half (45.7%) of the total. Japan, the UK, Australia, Finland, and Canada also invested heavily in this field with no less than 5% contribution of the total, respectively. Ranking the quality of papers on basis of *h*-index, the highest rank was received by the USA, followed by Germany and the UK. China only had a rank of seventh.

Collaboration type was determined by the addresses of authors, where the term “international collaboration” was designated if researchers’ addresses were from different countries. The USA ranked 1st based on the international collaborative publications and 16th in terms of international collaborative rate (32.7%). Sweden with lower article output had the highest international collaborative rate. On the contrary, China with the second-highest article output had the lowest international collaborate rate. If just looking at the *h*-index of the international collaborative publications, the top three countries were the USA, Germany and Finland. China only ranked ninth.

To evaluate the contribution of institutes, articles whose author addresses originated from the same institutes were assigned “single-institute articles.” In total, 1,741 institutes in worldwide and 231 in China devoted to the microcystin research. Table 2 shows the top 17 institutes in worldwide with no less than 30 article output and in China with no less than 6 article output from 1991 to 2011. For worldwide research, 37.2% of the 2,824 articles were published by the top 17 institutes, which came from 11 countries: 3 Germany, 3 UK, 2 USA, 2 Japan, 1 China, 1 Finland, 1 Canada, 1 Czech Republic, 1 Australia, 1 Portugal, and 1 Brazil. One institute of China, Chinese Academy of Sciences (CAS), came top in article output, single-institute article number, and percentage. However, it only had a rank of sixth based on *h*-index. For China research, the articles of the top 17 institutes accounted for 96.3%. Almost half of the total were published by the CAS. It also topped the ranking of *h*-index and single-institute articles. The article outputs of the other 16 institutes were all far behind that of the CAS. Zhejiang Univ. ranked first in single-institute article percentage.

3.3. Publication distribution of subject categories and journals

The worldwide microcystin articles were included in 56 subject categories. Chinese researchers participated in 46 categories. The top 12 subject categories in worldwide with no less than 103 articles and in China

with no less than 12 articles are demonstrated in Table 3. For worldwide research, 27.1% articles were included in Toxicology, followed by Environmental Sciences Ecology and Pharmacology Pharmacy. The Toxicology, Biochemistry Molecular Biology, and Environmental Sciences Ecology are the top three in terms of *h*-index. For China research, 42.8% articles were included in Environmental Sciences Ecology, followed by Toxicology and Chemistry. The top three were Toxicology, Environmental Sciences Ecology, and Pharmacology Pharmacy based on *h*-index.

Worldwide 2,824 and in China 400 articles were published in 598 and 154 journals, respectively, including specialty journals and journals of other disciplines. Table 4 lists the top 11 journals. Obviously, the specialty journals published the most articles. *Toxicol* and *Environmental Toxicology* ranked first and second in both worldwide and China in terms of article numbers. Interestingly, the top 11 journals of world and China showed similar ranking orders based on *h*-index and IF.

3.4. Distribution analysis of author keywords

To further evaluate the research trends, the information that is closer to the research itself, author keywords were also analyzed. These words straightly supply readers with research focus that the authors are interested in and the internal structure of authors reasoning. Therefore, they are excellent to mine the information about the research trends.

To precisely and completely analyze the keywords, those words with identical meanings or being misspelled were grouped and considered as a single word. For example, the keywords “cyanobacteria,” “cyanobacterium,” and “blue green algae” were reclassified as “cyanobacteria.” Then, these normalized keywords were ranked according to their frequencies. To study the development trends in different periods, these keywords in the past 21 years were separated into three independent seven-year periods: 1991–1997 (P1), 1998–2004 (P2), and 2005–2011 (P3). Their growth rates were calculated by frequencies of P2/P1 and frequencies of P3/P2. Since there were only two articles published during the P1 of China, the keywords in this period were no longer analyzed. To quantitatively evaluate the grow rate of keywords, they were classified into four groups: explosive hotspots (growth rate >5), hotspots (growth rate ≥ 1.2 and ≤ 5), general hotspots (growth rate >0.8 and <1.2), and out of the mainstream hotspots (growth rate ≤ 0.8). Some keywords appeared in P2 or P3 for the first time, whose growth rates could not be calculated. They were regarded as explosive hotspots.

Table 2
Top 17 most productive institutes worldwide and in China, 1991–2011

Institute	Worldwide			China		
	Total articles No. (percentage of all articles)	<i>h</i> -index (rank)	Single-institute articles No. (percentage of articles from institute)	Total articles No. (percentage of all articles)	<i>h</i> -index (rank)	Single-institute articles No. (percentage of articles from institute)
Chinese Acad. Sci. (China)	197 (7.0)	24 (6)	97 (49.2)	197 (49.3)	24 (1)	97 (49.2)
Univ. Dundee (the UK)	105 (3.7)	42 (1)	21 (20)	28 (7.0)	12 (2)	8 (28.6)
Univ. Helsinki (Finland)	87 (3.1)	34 (3)	18 (20.7)	24 (6.0)	8 (4)	1 (4.2)
Abo Akad Univ. (the UK)	71 (2.5)	25 (5)	15 (21.1)	23 (5.8)	9 (3)	18 (78.3)
Wright State Univ. (the USA)	66 (2.3)	36 (2)	7 (10.6)	20 (5.0)	8 (4)	4 (60)
Meijo Univ. (Japan)	64 (2.3)	30 (4)	3 (4.7)	14 (3.5)	9 (3)	3 (21.4)
Univ. Alberta (Canada)	48 (1.7)	30 (4)	13 (27.1)	11 (2.8)	6 (5)	2 (18.2)
Masaryk Univ. (Czech Republic)	48 (1.7)	12	5 (10.4)	10 (2.5)	5 (6)	1 (10)
Univ. Illinois (the USA)	46 (1.6)	30 (4)	9 (19.6)	10 (2.5)	4 (7)	7 (70)
Univ. New S Wales (Australia)	46 (1.6)	25 (5)	9 (19.6)	8 (2.0)	8 (4)	0 (0)
Humboldt Univ. (Germany)	43 (1.5)	30 (4)	5 (11.6)	7 (1.8)	6 (5)	0 (0)
Nat. Inst. Environ. Studies (Japan)	43 (1.5)	21 (8)	9 (20.9)	7 (1.8)	3 (8)	1 (14.3)
Univ. Porto (Portugal)	42 (1.5)	10	7 (16.7)	7 (1.8)	3 (8)	5 (71.4)
Leibniz Inst Freshwater Ecol & Inland Fisheries (Germany)	41 (1.5)	14	15 (36.6)	7 (1.8)	3 (8)	0 (0)
Tech. Univ. Berlin (Germany)	37 (1.3)	23 (7)	0 (0)	6 (1.5)	4 (7)	0 (0)
Robert Gordon Univ. (the UK)	36 (1.3)	17 (9)	12 (33.3)	6 (1.5)	4 (7)	0 (0)
Univ. Sao Paulo (Brazil)	30 (1.1)	9 (15)	4 (13.3)	6 (1.5)	2 (9)	0 (0)

Table 3
Top 12 subject categories worldwide and in China, 1991–2011

Worldwide			China		
Subject category	Articles (%)	<i>h</i> -index (rank)	Subject category	Articles (%)	<i>h</i> -index (rank)
Toxicology	764 (27.1)	65 (1)	Environmental Sciences Ecology	171 (42.8)	20 (2)
Environmental Sciences Ecology	730 (25.8)	55 (3)	Toxicology	134 (33.5)	24 (1)
Pharmacology Pharmacy	421 (14.9)	52 (4)	Chemistry	86 (21.5)	15 (4)
Marine Freshwater Biology	419 (14.8)	45 (6)	Pharmacology Pharmacy	48 (12)	18 (3)
Biochemistry Molecular Biology	401 (14.2)	57 (2)	Engineering	40 (10)	9 (7)
Chemistry	401 (14.2)	41 (7)	Marine Freshwater Biology	36 (9)	12 (5)
Water Resources	325 (11.5)	45 (6)	Water Resources	36 (9)	10 (6)
Engineering	254 (9)	40 (8)	Biochemistry Molecular Biology	35 (8.8)	10 (6)
Microbiology	225 (8)	49 (5)	Science Technology—Other Topics	24 (6)	8 (8)
Biotechnology Applied Microbiology	166 (5.9)	40 (9)	Materials Science	13 (3.3)	6 (9)
Plant Sciences	105 (3.7)	28 (11)	Biotechnology Applied Microbiology	13 (3.3)	6 (9)
Cell Biology	103 (3.6)	39 (10)	Fisheries	12 (3)	6 (9)

Table 4
Top 11 journals worldwide and in China, 1991–2011

Worldwide				China			
Journal title	Articles (%)	<i>h</i> -index (rank)	IF (rank)	Journal title	Articles (%)	<i>h</i> -index (rank)	IF (rank)
Toxicicon	275 (9.7)	43 (1)	2.508 (8)	Toxicicon	33 (8.3)	17 (1)	2.508 (5)
Environmental Toxicology	152 (5.4)	29 (4)	2.407 (9)	Environmental Toxicology	26 (6.5)	9 (2)	2.407 (6)
Water Research	80 (2.8)	31 (3)	4.865 (2)	Bulletin of Environmental Contamination and Toxicology	13 (3.3)	6 (4)	3.206 (4)
Applied and Environmental Microbiology	58 (2.1)	31 (3)	3.829 (5)	Chemosphere	13 (3.3)	7 (3)	1.018 (9)
Journal of Biological Chemistry	57 (2.0)	36 (2)	4.773 (3)	Journal of Environmental Sciences—China	10 (2.5)	3 (6)	1.66 (8)
Harmful Algae	49 (1.7)	12 (9)	3.083 (7)	Chinese Journal of Analytical Chemistry	10 (2.5)	3 (6)	0.941 (10)
Environmental Science Technology	48 (1.7)	20 (6)	5.228 (1)	Fresenius Environmental Bulletin	9 (2.3)	2 (7)	4.173 (2)
Aquatic Toxicology	48 (1.7)	25 (5)	3.761 (6)	Journal of Hazardous Materials	9 (2.3)	4 (5)	0.66 (11)
Chemosphere	35 (1.2)	13 (8)	1.018 (11)	Ecotoxicology	8 (2)	3 (6)	2.355 (7)
Journal of Chromatography A	34 (1.2)	19 (7)	4.531 (4)	Environmental Pollution	7 (1.8)	7 (3)	4.555 (1)
Hydrobiologia	33 (1.2)	12 (9)	1.784 (10)	Analytica Chimica Acta	7 (1.8)	6 (4)	3.746 (3)

Table 5 lists the top 30 most used keywords that appeared in worldwide microcystin articles and their growth rates. According to the criteria, the “Oxidative Stress,” “Biodegradation,” and “Degradation” were the explosive hotspots, “Toxins,” “Hepatotoxins,” and “Hepatotoxicity” were the out of the mainstream hotspots. “Protein Phosphatase” and “Okadaic Acid” were the general hotspots. All the others were the hotspots.

The top 30 most used keywords in Chinese researchers’ articles are shown in Table 6. The “Lake Tai,” *Microcystis*, “Real-Time PCR,” “Reactive oxygen species,” “Silver carp,” “Gene expression,” “Growth,” “PP2A,” “Ultrastructure,” “Superoxide dismutase (SOD),” “Kinetics,” “Adsorption,” “Bighead carp,” and “Catalase” (CAT) could not be seen in the worldwide top 30. So, the research trends of China are

different from other countries. In addition, 16 keywords appeared for the first time in P3. They were all considered as explosive hotspots. The others were all hotspots or general hotspots.

4. Discussion

The microcystin research trends in China and worldwide were compared by analyzing the yearly article output, cumulative number of articles, distribution of countries, institutes, subject categories, and journals, as well as by analyzing author keywords from 1991 to 2011. Some significant results have been obtained, which will provide scientists with a clear picture of the current research status and the future directions in the microcystin research.

Table 5
Top 30 frequency of author keywords used in worldwide microcystin articles with their growth rates, 1991–2011

Author keyword	1991–2011	1991–1997 (P1)	1998–2004 (P2)	2005–2011 (P3)	P2/P1	P3/P2
Microcystins	960	60	268	632	4.5	2.4
Cyanobacteria	651	61	213	377	3.5	1.8
MC-LR	311	29	87	195	3.0	2.2
Cyanotoxins	215	7	79	129	11.3	1.6
<i>Microcystis aeruginosa</i>	149	12	37	100	3.1	2.7
Nodularin	106	12	43	51	3.6	1.2
Toxins	94	11	48	35	4.4	0.7
Protein phosphatase	74	34	22	18	0.6	0.82
Toxicity	74	6	25	43	4.2	1.7
Hepatotoxins	70	25	29	16	1.2	0.6
Oxidative Stress	67	0	6	61	–	10
Apoptosis	63	0	18	45	–	2.5
Fish	62	0	11	51	–	4.6
ELISA	57	1	19	37	19.0	1.9
Cylindrospermopsin	51	0	16	35	–	2.2
HPLC	45	5	11	29	2.2	2.6
Liver	44	1	18	25	18.0	1.4
Okadaic Acid	42	19	11	12	0.6	1.1
Anatoxin A	41	3	9	29	3.0	3.2
Drinking water	39	4	14	21	3.5	1.5
Microcystin-RR	39	3	6	30	2.0	5.0
Blooms	38	5	8	25	1.6	3.1
Biodegradation	36	2	5	29	2.5	5.8
Cyanobacterial blooms	35	0	8	27	–	3.4
Eutrophication	34	0	8	26	–	3.3
Degradation	29	1	4	24	4.0	6.0
Planktothrix	29	0	8	21	–	2.6
Glutathione S-transferase	28	0	12	16	–	1.3
Water treatment	28	0	12	16	–	1.3
Hepatotoxicity	26	5	13	8	2.6	0.6

Note: “–” indicate that the growth rates of the keywords could not be calculated, since they emerged for the first time.

Table 6
Top 30 frequency of author keywords used in China microcystin articles with their growth rates, 1991–2011

Author keyword	1991–2011	1998–2004 (P2)	2005–2011 (P3)	P3/P2
Microcystins	163	22	141	6.4
MC-LR	77	7	70	10.0
Cyanobacteria	33	6	25	4.2
Microcystin-RR	28	1	27	27.0
<i>Microcystis aeruginosa</i>	26	0	26	–
Apoptosis	24	0	24	–
Lake Tai	20	1	19	19.0
<i>Microcystis</i>	15	1	14	14.0
Oxidative stress	15	0	15	–
Cyanobacterial blooms	14	3	11	3.7
Degradation	13	0	13	–
Real-Time PCR	13	0	13	–
Toxicity	12	4	8	2.0
ROS	10	3	7	2.3
Silver carp	11	0	11	–
Biodegradation	10	1	9	9.0
Gene expression	10	0	10	–
Growth	9	1	8	8.0
Liver	9	0	9	–
Eutrophication	8	1	7	7.0
PP2A	8	0	8	–
Ultrastructure	8	0	8	–
SOD	8	2	6	3.0
Fish	7	0	7	–
Kinetics	7	0	7	–
HPLC	7	1	6	6.0
Adsorption	6	1	5	5.0
Bighead carp	6	0	6	–
CAT	6	1	5	5.0
Glutathione S-transferase	6	0	6	–

Note: “–” indicate that the growth rates of the keywords could not be calculated, since they emerged for the first time.

Since 2001, increasing numbers of articles referring to microcystins were published by Chinese researchers, the growth rate of which was higher than that of the worldwide. Such growth was accompanied by the scientific and technological progress and economic development of China, however, at the expense of the serious environmental pollution and ecological destruction [17,19]. Eutrophication of fresh water bodies has resulted in the increasing frequency of cyanobacterial blooms. So, the hazard metabolites of them, microcystins, have become the new focus. China's cumulative number of microcystin articles increased very fast. It could be predicted that the cumulative number of scientific papers on microcystins in 2013 will be twice of that in 2011 based on the perfect exponential models. However, it will need 12 years for the worldwide cumulative number of

articles to double of that in 2011. Undoubtedly, the growth rate of the cumulative number of articles of China is faster than that of the worldwide.

The 2,824 articles were published by 80 countries or territories, showing that the microcystins have come into the research focus of many countries. The top 10 countries showed no obvious difference in the article output, indicating that these countries all attached great importance to this issue and consistently devoted considerable manpower and material resources to that end. It is also suggested that this bloom issue is serious in many countries [1]. Although China ranked second in article output, the visibility of these papers was relatively lower. The rank of its international collaborative rate was the 20th. China may benefit from more collaboration with the USA, Germany, Finland, the UK, Japan, and Australia

which had higher *h*-index in both article output and international collaborative ones.

The CAS of China ranked first in terms of total articles and single-institute articles both in China and worldwide. It is the biggest research institute in China with 12 branch offices, 117 institutes, more than 100 national key laboratories and national engineering research centers, and about 1,000 field stations throughout the country. Its staff even surpassed 50,000. The top nine productive authors devoting themselves to the microcystin research were all from this institute (data not shown). It is not surprising that so many articles were published by the CAS. However, the *h*-index of it was not in proportion to its total article output. It could be helpful for CAS to collaborate with other institutes with higher *h*-index. In addition, the total article outputs of the other 16 institutes were still lower than that of the CAS. More fund allocation and more collaboration may be helpful for them.

There were also positive aspect of microcystin research in China; the top three journals with the most articles published by Chinese researchers had higher IF and *h*-index rank. The microcystin research of China is comparable with that of the worldwide based on the IF.

Author keywords analysis revealed the current hotspots and explosive hotspots of worldwide microcystin research, which could be mainly divided into five categories: (a) Categories of toxins. “Microcystin-LR” and “Microcystin-RR” are the major “Microcystins.” “Microcystin-LR,” “Nodularin,” and “Cylindrospermopsin” are three kinds of well-studied hepatotoxins due to their potential carcinogenicity [6]. “Anatoxin-A” belongs to neurotoxin [30]. All these toxins mentioned belong to “Cyanotoxins.” (b) Sources of toxins. The “Blooms,” especially “Cyanobacterial blooms” induced by “Eutrophication” are the main sources of cyanotoxins. *M. aeruginosa* and *Planktothrix* are the main sources of microcystins and “Anatoxin-A,” respectively [6]. (c) Hazard of toxins. Microcystins can cause both acute and chronic “Toxicity” in “Fish” and other aquatic animals and make the “Drinking water” unavailable. The “Oxidative Stress” caused by microcystins can cause the “Apoptosis” of mammal cells [14,15]. (d) Detection of toxins. “ELISA” (Enzyme linked immunosorbent assays) is the main method to detect toxins [31]. (e) Removal of toxins. “Biodegradation,” “Degradation,” and “Water treatment” were applied to remove the toxins in drinking water. In addition, glutathione S-transferases are also important for the detoxification of microcystins [32]. It is obvious that the group a categories of toxins attracted the most attention.

China’s top 30 keywords were all hotspots and explosive hotspots, which can also be divided into five categories: (a) Categories of toxins. Only “Microcys-

tins,” “Microcystin-LR,” and “Microcystin-RR” appeared in the China list. Other cyanotoxins were not highlighted by Chinese researchers. (b) Sources of toxins. *Microcystis* also appeared in the China list besides of “Cyanobacteria,” *M. aeruginosa*, “Cyanobacterial blooms,” and “Eutrophication.” (c) Hazard of toxins. Except for “Apoptosis,” “Oxidative Stress,” “Toxicity,” and “Fish,” Chinese researchers also paid great attention to the effects of microcystins on the “Lake Tai,” the damage to the “liver” and kidney of “Bighead carp,” the evoking of the harmful “Reactive oxygen species,” the impaired “Growth” of cells, the inhibition to “PP2A,” the “Kinetics” of DNA damage, the change of cell “Ultrastructure,” and the activities of hepatic antioxidant enzymes including “Catalase” and “Superoxide dismutase,” and the alterations of “gene expression” [18,33–37]. (d) Detection of toxins. “HPLC” (High-performance liquid chromatography) and “Real-Time PCR” were used to identify microcystins and analyze the change of gene expressions due to the microcystins [38,39]. (e) Removal of toxins. “Adsorption” was also widely used to counteract cyanotoxin contamination in China except for “Biodegradation” and “Degradation” and “Glutathione S-transferase.” It could be easily concluded that Chinese researchers paid the most attention to group c, the hazard of the toxins.

The explosive hotspots “Oxidative Stress,” “Biodegradation,” and “Degradation” will be the worldwide new research directions. The hotspots will go on attracting more attention. Some keywords have become general hotspots or out of the mainstream hotspots, which can be attributed to two aspects: (a) some have been best studied and widely recognized, such as “Toxins” and “Hepatotoxins”. (b) Some general words were replaced by more specific words; for example, “Protein phosphatase” had been replaced by more specific “Protein phosphatase 1” and “Protein phosphatase 2A.”

Among the explosive hotspots of China microcystin research that is different from that of the worldwide, “Lake Tai” and *Microcystis* ranked first and second in terms of frequencies in P3 and growth rates. So, they will be China’s specific research directions. Two aspects may account for this: (a) the Chinese researchers devoted themselves more to the local “Lake Tai” issue. (b) Some worldwide hotspots were overlooked by Chinese researchers, such as “Anatoxin-A” and “Cylindrospermopsin,” due to limited financial and manpower resources.

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References

- [1] G.M. Hallegraeff, A review of harmful algal blooms and their apparent global increase, *Phycologia* 32 (1993) 79–99.
- [2] G. Badiaa, G. Djamel, S. Ali, Algae and cyanotoxins removal by coagulation/flocculation: A review, *Desalin. Water Treat.* 20 (2010) 133–143.
- [3] A.D. Ferrao, B. Kozlowsky-Suzuki, Cyanotoxins: Bioaccumulation and effects on aquatic animals, *Mar. Drugs* 9 (2011) 2729–2772.
- [4] D.R. de Figueiredo, U.M. Azeiteiro, S.M. Esteves, F.J.M. Gonçalves, M.J. Pereira, Microcystin-producing blooms—A serious global public health issue, *Ecotox. Environ. Safe* 59 (2004) 151–163.
- [5] M.E. van Apeldoorn, H.P. van Egmond, G.J. Speijers, G.J.I. Bakker, Toxins of cyanobacteria, *Mol. Nutr. Food Res.* 51 (2007) 7–60.
- [6] B. Zegura, A. Straser, M. Filipič, Genotoxicity and potential carcinogenicity of cyanobacterial toxins—A review, *Mutat. Res.* 727 (2011) 16–41.
- [7] E. Dittmann, C. Wiegand, Cyanobacterial toxins—Occurrence, biosynthesis and impact on human affairs, *Mol. Nutr. Food Res.* 50 (2006) 7–17.
- [8] W.W. Carmichael, V.R. Beasley, D. Bunner, J. Eloff, I. Falconer, P. Gorham, K.-I. Harada, M.-J. Yu, T. Krishnamurthy, R.E. Moore, K.L. Rinehart, M.T. Runnegar, O.M. Skullberg, M. Watanabe, Naming of cyclic heptapeptide toxins of cyanobacteria (blue-green algae), *Toxicon* 26 (1988) 971–973.
- [9] N. Gupta, S.C. Pant, R. Vijayaraghavan, P.V.L. Rao, Comparative toxicity evaluation of cyanobacterial cyclic peptide toxin microcystin variants (LR, RR, YR) in mice, *Toxicology* 188 (2003) 285–296.
- [10] I. Chorus, *Cyanotoxins: Occurrence, Causes, Consequences*, Springer Verlag, Berlin, 2001.
- [11] B.C. Hitzfeld, S.J. Hoger, D.R. Dietrich, Cyanobacterial toxins: Removal during drinking water treatment and human risk assessment, *Environ. Health Perspect.* 108 (2000) 1113–1122.
- [12] J.T. Maynes, H.A. Luu, M.M. Cherney, R.J. Andersen, D. Williams, C.F.B. Holmes, M.N.G. James, Crystal structures of protein phosphatase-1 bound to motuporin and dihydromicrocystin-LA: Elucidation of the mechanism of enzyme inhibition by cyanobacterial toxins, *J. Mol. Biol.* 356 (2006) 111–120.
- [13] R. Nishiwaki-Matsushima, T. Ohta, S. Nishiwaki, M. Suganuma, K. Kohyama, T. Ishikawa, W.W. Carmichael, H. Fujiki, Liver tumor promotion by the cyanobacterial cyclic peptide toxin microcystin-LR, *J. Cancer Res. Clin. Oncol.* 118 (1992) 420–424.
- [14] W.X. Ding, H.M. Shen, C.N. Ong, Critical role of reactive oxygen species and mitochondrial permeability transition in microcystin-induced rapid apoptosis in rat hepatocytes, *Hepatology* 32 (2000) 547–555.
- [15] H. Zhang, J. Zhang, Y. Chen, Y. Zhu, Microcystin-RR induces apoptosis in fish lymphocytes by generating reactive oxygen species and causing mitochondrial damage, *Fish Physiol. Biochem.* 34 (2008) 307–312.
- [16] X. Song, Enhanced treatment of polluted surface water from Yellow River (China) with bio-oxidation as pretreatment: Pilot scale studies, *Desalin. Water Treat.* 9 (2009) 59–65.
- [17] J. Luo, J.F. Ying, L. Cai, K. Zhang, K.D. Hyde, Freshwater fungi in Lake Dianchi, a heavily polluted lake in Yunnan, China, *Fungal Divers.* 16 (2004) 93–112.
- [18] L. Song, W. Chen, L. Peng, N. Wan, N. Gan, X. Zhang, Distribution and bioaccumulation of microcystins in water columns: A systematic investigation into the environmental fate and the risks associated with microcystins in Meiliang Bay, Lake Taihu, *Water Res.* 41 (2007) 2853–2864.
- [19] J.H. Qu, M.H. Fan, The current state of water quality and technology development for water pollution control in China, *Crit. Rev. Environ. Sci. Tech.* 40 (2010) 519–560.
- [20] S. Lin, J. Shen, Y. Liu, X. Wu, Q. Liu, R. Li, Molecular evaluation on the distribution, diversity, and toxicity of *Microcystis* (Cyanobacteria) species from Lake Ulungur—A mesotrophic brackish desert lake in Xinjiang, China, *Environ. Monit. Assess.* 175 (2011) 139–150.
- [21] W. Qin, L. Yang, X. Zhang, Z. Zhang, L. Xu, J. Wu, J. An, Y. Wang, Cyanobacteria—Blooming water samples from Lake Taihu induce endoplasmic reticulum stress in liver and kidney of mice, *Ecotoxicology* 21 (2012) 1495–1503.
- [22] B. Qin, G. Zhu, Y. Zhang, W. Li, H.W. Paerl, W.W. Carmichael, G. Gao, A drinking water crisis in Lake Taihu, China: Linkage to climatic variability and lake management, *Environ. Manage.* 45 (2010) 105–112.
- [23] S.Z. Yu, Drinking water and primary liver cancer, In: Z.Y. Tang, M.C. Wu, S.S. Xia (Eds.), *Primary Liver Cancer*, Berlin and China Academic Publications, Beijing, pp. 30–37, 1989.
- [24] Y. Ueno, S. Nagata, T. Tsutsumi, A. Hasegawa, M.F. Watanabe, H.-D. Park, G.-C. Chen, G. Chen, S.-Z. Yu, Detection of microcystins, a blue-green algal hepatotoxin, in drinking water sampled in Haimen and Fusui, endemic areas of primary liver cancer in China, by highly sensitive immunoassay, *Carcinogenesis* 17 (1996) 1317–1321.
- [25] S.D. Xie, J. Zhang, Y.S. Ho, Assessment of world aerosol research trends by bibliometric analysis, *Scientometrics* 77 (2008) 113–130.
- [26] J.F. Li, Y.H. Zhang, X.S. Wang, Y.-S. Ho, Bibliometric analysis of atmospheric simulation trends in meteorology and atmospheric science journals, *Croat. Chem. Acta* 82 (2009) 695–705.
- [27] O.D. Persson, R. Danell, J. Wiborg Schneider, How to use Bibexcel for various types of bibliometric analysis, In: F. Åström, R. Danell, B. Larsen, J. Schneider (Eds.), *Celebrating Scholarly Communication Studies: A Festschrift for Olle Persson at his 60th Birthday*, International Society for Scientometrics and Informetrics, Leuven, pp. 9–24, 2009.
- [28] J.E. Hirsch, An index to quantify an individual's scientific research output, *Proc. Nat. Acad. Sci.* 102 (2005) 16569–16572.
- [29] J.E. Hirsch, Does the H index have predictive power? *Proc. Nat. Acad. Sci.* 104 (2007) 19193–19198.
- [30] J.P. Devlin, O.E. Edwards, P.R. Gorham, N.R. Hunter, R.K. Pike, B. Stavric, Anatoxin—A, a toxic alkaloid from *Anabaena flos-aquae* NRC-44h, *Can. J. Chem.* 55 (1977) 1367–1371.
- [31] F.S. Chu, X. Huang, R.D. Wei, W.W. Carmichael, Production and characterization of antibodies against microcystins, *Appl. Environ. Microbiol.* 55 (1989) 1928–1933.
- [32] L. Hao, P. Xie, J. Fu, G. Li, Q. Xiong, H. Li, The effect of cyanobacterial crude extract on the transcription of GST mu, GST kappa and GST rho in different organs of goldfish (*Carassius auratus*), *Aquat. Toxicol.* 90 (2008) 1–7.
- [33] L. Li, P. Xie, L. Guo, Z. Ke, Q. Zhou, Y. Liu, T. Qiu, Field and laboratory studies on pathological and biochemical characterization of microcystin-induced liver and kidney damage in the phytoplanktivorous bighead carp, *Sci. World J.* 8 (2008) 121–137.
- [34] Y. Li, P. Xie, T. Qiu, H.-Y. Li, G.-Y. Li, L. Hao, Q. Xiong, Microcystin extracts induce ultrastructural damage and biochemical disturbance in male rabbit testis, *Environ. Toxicol.* 25 (2010) 9–17.
- [35] J. Jiang, X. Gu, R. Song, X. Wang, L. Yang, Microcystin-LR induced oxidative stress and ultrastructural alterations in mesophyll cells of submerged macrophyte *Vallisneria spiralis* (Lour.) Hara, *J. Hazard Mater.* 190 (2011) 188–196.
- [36] N. Bouaicha, I. Maatouk, Microcystin-LR and nodularin induce intracellular glutathione alteration, reactive oxygen species production and lipid peroxidation in primary cultured rat hepatocytes, *Toxicol. Lett.* 148 (2004) 53–63.
- [37] J. Fu, P. Xie, The acute effects of microcystin LR on the transcription of nine glutathione S-transferase genes in common carp *Cyprinus carpio* L., *Aquat. Toxicol.* 80 (2006) 261–266.

- [38] S. Lin, J. Shen, Y. Liu, X. Wu, Q. Liu, R. Li, Molecular evaluation on the distribution, diversity, and toxicity of *Microcystis* (Cyanobacteria) species from Lake Ulungur—A mesotrophic brackish desert lake in Xinjiang, China, *Environ. Monit. Assess.* 175 (2011) 139–150.
- [39] G. Li, P. Xie, H. Li, L. Hao,, Q. Xiong, T. Qiu, Y. Liu, Acute effects of microcystins on the transcription of 14 glutathione S-transferase isoforms in Wistar rat, *Environ. Toxicol.* 26 (2011) 187–194.