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Worldwide Scientific Trends on Ochratoxin-A During 1965–2016

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Abstract

The contamination in foodstuff by ochratoxin A (OTA) has become a major problem to humans and animals. Hence, many countries have expressed interest on researching OTA. However, the current development trends of OTA are not well understood. This study discussed the research trends and hotspots of OTA and investigated the contribution of research from seven areas: countries, institutions, authors, publications, subject categories, keywords and journals. Related publications on OTA during 1965-2016 were retrieved from the Web of Science database. CiteSpace V and bibliometric technologies combined with network analysis were used in exploring research hotspots and basic statistics of OTA. A total of 4889 articles, which were contributed from 103 countries, were identified. Most countries are from Europe, such as Italy, Germany and France. The USA, which ranks first, accounts for 11.1% of the articles with 543 records. Additionally, the top three high-cited countries are Denmark, the Netherlands and Austria, all from Europe. Surprisingly, China has a large number of publications which accounts for 6 but lesser citation scores. In the subject of nutrition and dietetics, keywords 'aptamer' and 'biosensor' are emerging, which are of increasing concern. This finding indicated that the literature growth in the field of OTA would be expanding rapidly in the future. European countries are the most influential countries, especially Denmark, the Netherlands and Austria. New technologies for detecting and identifying OTA as well as nutrition and dietetics would be paid more attention by scholars or the society.

Keywords: Ochratoxin A; Food contamination; Bibliometric analysis; Research trends; Nutrition and dietetics; Aptamer and biosensor

Introduction

With the increasing awareness on healthy diet, more and more people pay attention to the security of food. Ochratoxin A (OTA, C20H18O6NCI) is the most important mycotoxin like aflatoxins from Aspergillus species and is one of the most toxic metabolites produced by various Aspergillus and Penicillium species [1-4]. OTA can breed at 15 and 15%-19% humidity in grains [5,6], such as corn, strain and wheat, and also in edible medicinal plants, such as glycyrrhizae radix et rhizome and Panax ginseng. Additionally, OTA is found in some plant products, such as grape wine, spices and coffee [7]. In animalderived food, pork products and milk of cows are the main sources of this toxin [1]. OTA exerts carcinogenic, immunotoxic and teratogenic effects on rats and likewise poses health hazards to humans [8-13]. Balkan endemic nephropathy is the most common disease caused by OTA. Hence, publications on technologies for the detection and identification of OTA have high-performance emerged. In the past, liquid chromatography, enzyme-linked immunosorbent assay and mass spectrometry were applied to detect OTA. However, these methods are expensive, time consuming and require specific sophisticated instruments. Owing to these disadvantages, some emerging technologies have been developed. Electrochemical aptasensors and aptamer-based sensors are typical and widespread technologies which have been recently applied to food toxin detection owing to their rapid detection and exceptional sensitivity. Seved Mohammad Taghdisia designed a novel fluorescent aptasensor based on gold nanoparticles for detecting OTA, and this technology has been successfully utilized on grape juice. Yang determined OTA in corn using fabricated instrument with а electrochemiluminescence biosensor, aptamer and hyperbranched rolling circle amplification and studied its stability, reproducibility and selectivity. They also indicated that the technology could produce good results and be used in food safety control [14-17]. On the basis of the health risks involved with OTA, the International Agency for Research on Cancer has grouped OTA as IIB carcinogen. The Committee on Food Additives and Contaminants of the World Health Organization established the maximum limit standard in 1997, that is, 5 µg in 1 kg of grain products to decrease hazard to humans. In 2006, the European Union passed a legislation implementing the maximum limitation of OTA in a certain number of products [18].

However, the current research situation, potential hotspots and development trends on OTA remain undetermined. In this study, we reveal the basic statistics and research hotspots related to OTA from seven aspects, including publications, countries, institutions, authors' contributions, subject categories, keywords and journals. We examine 4889 publications on the Web of Science (WoS) database from 1965 to 2016 by CiteSpace V software and bibliometrics methods combined with network analysis. We mainly evaluate the growth trend and quality of publications and the top 20 research countries. We summaries the current development trends on OTA by analyzing the burst detection of subject categories and keywords. Moreover, several suggestions for improving research situation are given.

Literature Review

Data and methods

We accessed the WoS database using the topic 'OTA' as the search term for collecting 4889 documents during 1965–2016. Each paper includes the title, authors, institutions, abstracts, keywords and cited references.

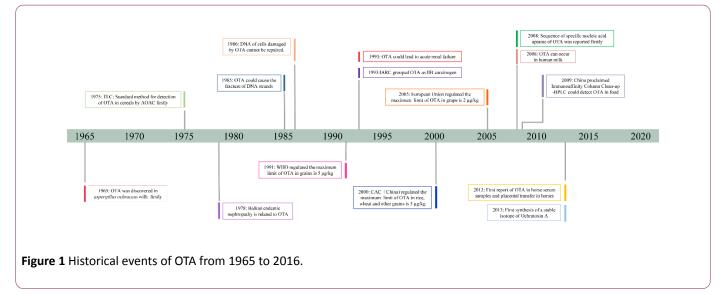
We utilized the information visualization software Cite Space V (Drexel University, Dr. Chaomei Chen) and traditional methods for the analysis of the following terms [19]:

Basic statistics: The publications and mean citation score per year, distributions of geography, main institutions, influential authors, top publishing journals, articles with highest impact factor and the most cited articles were covered, which can indicate the importance of OTA between different countries and stages. **Study hotspots:** Subject categories and keywords to investigate the hotspots and trends within the field were used. We analyzed main subject categories, capital keywords and their burst detection, which was used to measure bursts keywords or subject categories as indicators of emerging trends that may influence scholars' prospective research selections.

Results and Discussion

Historical events of OTA

We summarized the historical events of OTA from 1965 to 2016. We found a total of 15 important events and most of them could be grouped as regulations, contaminated resources, related diseases and detecting techniques. For example, in 1993, IARC grouped OTA as IIB carcinogens and researchers found that Balkan endemic nephropathy is related to OTA in 1978. In addition, WHO regulated the maximum limit of OTA in grains is 5 μ g/kg in 1991, CAC, an institution in china proclaimed the maximum limit of OTA in rice, wheat and other grains is 5 μ g/kg in 2000 and in 2005, European Union declared the maximum limit of OTA in grape is 2 μ g/kg. Hence, we can easily conclude that OTA's virulent is strong. Moreover, TIC and Immunoaffinity Column Clean-up combined HPLC regulated them as the standard methods for detecting OTA by AOAC and China respectively **Figure 1**.



Quantity of publications and growth trend

OTA-related literature published from 1965 to 2016 was obtained from the WoS database. A total of 4889 documents can be retrieved. Nearly all the papers were in English, which account for 95.91%, and others were in 14 different languages, led by German (1.82%), French (0.65%) and Portuguese (0.43%), all are mainly spoken in Europe. Some others were in Czech, Spanish and Chinese **Figure 2**.

Figure 2 shows the development on the number of publications by year, as well as the mean citation score per year. Based on the growth trend, the whole course can be roughly split into three stages. The early stage was in

1965-2010, which was characterized by a steady growth. However, the second stage in 2011-2012 witnessed that the trend fell sharply. During the last stage in 2013-2016, publications exponentially increased, which was caused by aflatoxin contamination in milk and dog food in 2013 throughout Europe and the USA, respectively. The published articles rose to 349 during 1965-2016, which indicates that OTA has become a popular topic in the scientific community. The trend shows that additional articles on OTA may be available in the coming years. Furthermore, the mean citation score can be divided into two stages with greater difference than the growth trend of publications. The first year (1965) was the first stage with the citation score of 542. Surprisingly,

in 1967, the decrease in the score of citation was notable from 542 to 59. Then, it showed a relatively steady state until 2016 with only 3.

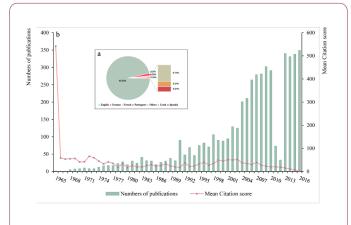
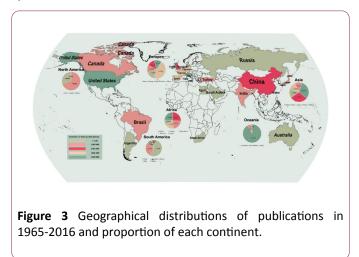


Figure 2 Publication and mean cited-frequency during 1965-2016 per year.

Countries' contributions to global publications

A total of 103 countries met the search criteria for OTA. **Figure 3** elucidates the geographical distribution of all papers on their representative countries. North America, Europe and Asia have published the majority of documents. In Europe, Italy accounted for approximately 14.07% followed by Germany (12.20%) and Spain (12.17%). In Asia, publications are primarily distributed in China (29.94%) followed by India (15.02%) and Japan (12.69%). The numbers of papers from North America were mostly from the USA (69.97%) and Canada (29.64%). The situation indicates that Europe always pays attention on healthy eating and that their food sources, such as milk, meat, corn and wheat, are easily contaminated by OTA.



We utilised the bibliometrics website (https:// bibliometric.com/) for examining the country collaboration network, as shown in **Figure 4**. The greater number of lines stretch out in one country, the stronger the cooperation with other countries. **Figure 4** shows that the top three countries with external cooperation are France, the USA and Italy. Some independent countries, such as Ukraine, Tanzania and Benin, have no cooperation. We hope that each country promotes international collaboration for reform and innovation in OTA development.

Figure 4 lists the top 20 productive countries, led by the USA, which published the most articles (543 records), followed by Italy (453 records) and Germany (393 records). However, the top three countries for mean citation score in OTA research were Denmark, the Netherlands and Austria, suggesting that they have published many high-quality papers. Interestingly, all of them are from Europe. China has published many articles of 321 records, which ranked sixth, but with lesser mean citation score like the top three countries. Hence, more efforts should be exerted to raise the influence of their publications.

Burst detection is a computational tool for identifying abrupt variations on events. The red line segment manifests the duration of change, and the count of strength indicates the intensity of change. The countries with the strongest citation bursts in the flied of OTA are listed in **Figure 4c**. The USA possessed the strength of 61.70 from 1965 to 1994. We conclude that the USA carried out a considerable amount of work on OTA during the time span. Unexpectedly, China had the highest strength of 81.56 from 2011 to 2016. We infer that OTA has attracted considerable attention, owing to aflatoxin contamination on the gutter oil and old oil and slop incidents that occurred in 2011. Scholars from Saudi Arabia, who contributed 16 papers, started showing more interest on OTA from 2013 to 2016.

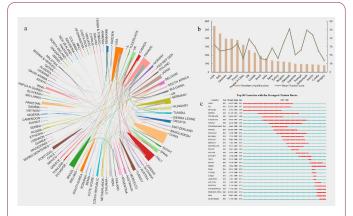


Figure 4 (a) Global cooperation; (b) the publication and mean cited-frequency of top 20 countries during 1965-2016; (c) 30 countries with burst detection.

Institution statistics

Figure 5 shows the main international collaborations between the main institutions. Results reveal that 4889 papers, which reflect the research on OTA, were distributed in 2961 institutions and have been watched extensively worldwide. **Figure 5** graphically presents that most institutions are from Europe, which corresponds to the data of the main research countries. In general, the larger the circle, the more the papers published by the institution [20], due to a potentially closer cooperation between institutions within the

same region. Hence, we conclude that the top three productive institutions were the University of Valencia (93 records), University of Wurzburg (85 records) and CNR (82 records) with the proportion of 1.90%, 1.74% and 1.68%, respectively. The collaboration in OTA research was mostly in the same geographic area such as INRA, University of Navarra and University of Bari (top-left corner), which are all from Europe. In China, China Agricultural University, Chinese Academy of Agricultural Sciences and Jiangnan University (middle-upper part) work closely with each other but with less relationships with foreign countries. Royal Institute of Technology has no collaboration with other institutions.

Figure 6 displays the burst detection of 52 institutions but with no higher strength among them. However, we found that burst detection started in 2013 in many institutions from Europe, North America and Asia. We implied that OTA became a pivotal topic due to the aflatoxin contamination in milk and dog food in 2013 throughout Europe and the USA, respectively. Chinese institutions have higher burst strength during 2013–2016, including China Agricultural University, Chinese Academy of Agricultural Sciences and Chinese Academy of Medical Sciences with the count of 19.34, 12.65 and 10.76.

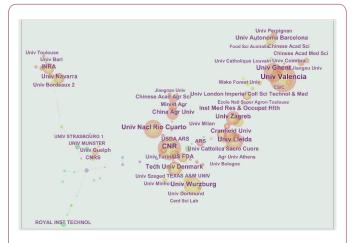
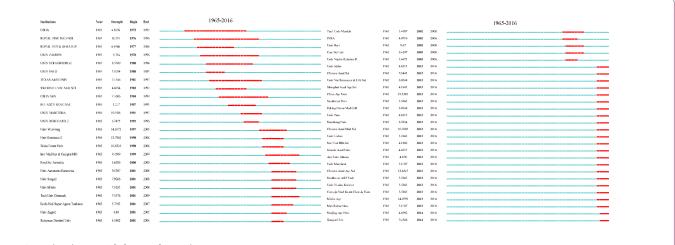


Figure 5 The collaboration patterns of institutions.



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Figure 6 Institutions with burst detection.

Author statistics

Results show that 4889 papers were produced by 10437 authors. **Figure 7** indicates the rankings of the top 20 fruitful authors who have 30 or more publications in this field. Of the top 20 productive authors, four are from France and four from Spain, both ranking the first, three are from Canada and two are from Germany. In addition, 95% of the top 20 authors except for Bacha H (Tunisia) come from European countries. Authors who published the most on OTA are Marin S and Sanchis V, each with 82 records and both from Spain. However, the top three authors with the highest citation score are Creppy EE, Pfohl-Leszkowicz A and Frisvad JC. Frisvad JC is the 14th productive author with 64 points in the mean citation score per article.

The burst detection of 48 authors is shown in **Figure 8**. The top 20 productive authors all exist in burst on OTA. Among them are three Spanish, namely, Marin S, Sanchis V and Ramos

AJ, with the strength of 17.32, 17.09 and 15.85, respectively, during 2004-2016.

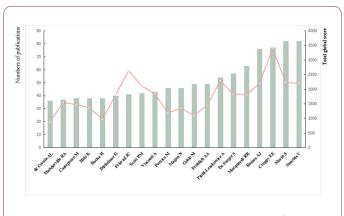


Figure 7 The publication counts and global cited-frequency of the top 20 authors.

Therefore, we speculate that many authors have jointly authored a ton of these articles, which is consistent with the

Subject category statistics

actual condition.

The subject categories can demonstrate which point is being focused on with a great concern currently on OTA. Our results revealed a wide range of subject categories on OTA with 94 counts, which remarkably cover food science and technology, chemistry and toxicology Figure 9, with 1625, 1273 and 1248 publications. They all can be classified as detection means and research with regard to OTA. The larger the purple ring (named centrality), the greater the transformation potential. As shown in Figure 9, the top three subject categories with transformation potential are biochemistry and molecular biology, microbiology and agriculture with the centrality of 1.18, 0.93 and 0.73, respectively, which are the essential research and the main source of OTA.

Figure 9 reveals the burst detection of 31 subject categories. We concluded that along with the situation of science and technological progress, other novel methods could be applied for determining OTA. Currently, electrochemistry and nanoscience and nanotechnology possess the highest burst strength of 20.10 and 15.49 from 2013 to 2016. Both are novel methods. Nutrition and dietetics also burst with 7.61 strength during 2014-2016, which illustrates that people around the world are increasingly concerned about food safety and healthy diet. Furthermore, with the increase in health awareness and economics, many research communities possibly pay more attention to the risk assessment of OTA on healthy eating.

a	b Subject Campories	Year Strength Bigle Bird 1965 - 2016
	BUTECHNOLOEN & APPLIED NICROBULOGY	1995 17300 1998 1995
	PATHY ON	1910 12-031 1979 1989
	DEVILOPMENTAL BIOLOGY	1985 18.3554 1974 1994
AGRICULTURE, DAIRY & ANIMAL SCIENCE	BIOLOGY	1005 4.065 1974 1951
	LIFE SCIENCES & ROMEDONE - OTHER 1000	3 196 4 193 193 198
	VETERINARY SCIENCES	1945 124302 1922 300
	AGREULTURE DAIRY & ANDIAL SCIENCE	1965 22.1276 (978-100)
MYCOLOGY AGRICULTURE	AGRICULTURE	1965 64259 1998 1959
	PHYSICLOGY	1965 1.3436 1982 2005
AGRICULTURE, MULTIDISCIPLINARY	00031067	1992 21.0054 1992 1991
	ENVIRONMENTAL SCIENCES & ECOLOGY	(565 a)(976 1984 159)
FOOD SCIENCE & TECHNOLOGY	ENVIRONMENTAL SCIENCES	1965 5.8005 1994 1985
VETERINARY SCIENCES	NEUROSCIENCES & NEUROLOGY	1945 4,5555 1947 2006
BIOCHEMISTRY & MOLECULAR BIOLOGY BIOCHEMICAL RESEARCH METHODS	NEEROSCHINGES	1945 4.5553 1997 2000
BIOCHEMISTRY & MOLECOLAR BIOLOGY BIOCHEMICAL RESEARCH METHODS	SOIL SCIENCE	1965 4.568 1990 1198
CHEMISTRY APPLIED	LINDLOGY & NEPTROLOGY	1085 23.096 1003 1009
	CILL BIOLOGY	1965 5.551 (983 2014
TOXICOLOGY CHEMISTRY	MICOLOGY	1965 x.631 1993 1995
	MEDICINE, RESEARCH & EXPERIMENTAL	1565 6.1332 1997 2006
CHEMISTRY, ANALYTICAL	AGRONOMY	1565 12.1371 1997 2005
	RESEARCH & EXPERIMENTAL MEDICINE.	1085 6.1332 1997 2256
BIOTECHNOLOGY & APPLIED MICROBIOLOGY	CHEMISTRY, APPLIED	1985 8.2824 3888 2000
	HOR DOUBTURE	1965 9,5963 3003 2500
MICROBIOLOGY	PRAEMACOLOGY & PRAEMACY	1965 6 2015 2003 2004
PHARMACOLOGY & PHARMACY	MICROBELOGY	1965 12.2357 2006 2007
PHARMACOLOGT & PHARMACT	SCIENCE & TECHNOLOGY - OTHER TOPICS	1965 178516 2012 2016
	ELECTROCHEMISTRY	1965 20.1005 2013 2016
	NANOSCIENCE & NANOTECINOLOGY	1961 154904 2013 2016
	DIOPHYSICS	1907 51408 2013 2016
	NUTRITION & DIFFETICS	1963 7.688 2014 2016

Figure 9 (a) The collaboration patterns of subject categories; (b) Subject categories with burst detection.

Keyword statistics

 Year Strength Begin
 End

 1965
 5.6201
 1967
 1993

 1965
 10.4358
 1973
 1989

 1965
 9.6063
 1973
 1982

 1965
 11.6
 1974
 1992

 1965
 11.6
 1974
 1992

 1965
 11.2
 1972
 1992

11.7743 1981 11.1192 1981

17.0651 1988 14.892 1988

16.9696 **1995** 14.0917 **1995**

10.9915 1996

9.4852 1998 2008

1965 11.9882 2001 2009

1965 11.0031 2001 2008

1965 10.5412 2001 2008

10.5204 2001 2010 9.1847 2001 2014 9.1573 2001 2008

9.1573 2001 2008 9.1443 2001 2008

8.6966 2001 2008 8.2362 2001 2008 12.7596 2002 2009

1965 11.7921 **2003**

1965 17.3151 2004 2016

1965 17.0873 2004 2016 1965 15.8536 2004 2016

5.2401 2004 2016 1965 10.1914 2005 2016

> 5.664 2006 2008

1965 12.2635 2007 2016

1965 11.9127 2013 2016

1965 11.9127 2013 2016

1965 10.3487 2013 2016

1965 8.2681 2013 2016

4.7052 2006 2016

8.249 2007 2010

7.3568 2010 2016

9.828 2013 2016

8,7877 2013 2016

Figure 8 authors with burst detection.

They are all from the University of Lleida, suggesting that

they might contribute more publications on OTA in the future.

Additionally, Huang KL, Wang Y and Xu WT are from China

Agricultural University, with an average strength of 11.39 during 2013-2016. Xu WT had the same strength as Huang KL.

965 10.1287 1998 9.938 1998 2012

9.5572 1995 2000 15.2048 1996 2005

Auti SCOTT PM HALD B KROGH P HUFF WE

KUBENA LF PHILLIPS TE

Creppy EE

Marquardt RR Frohlich AA Gekle M

Silbernagl S Castegnaro M Manderville RA

Pfohl-Leszk

Peraica M

Cabanes FJ

Domijan AM

Domijan AM Van Peteghem (Visconti A Verancio A Pietri A Varga J Bragulat MR Aburca ML Frisvad JC Dekant W Marin S Sanchis V

Sanchis V Ramos AJ de Cerain AL Magan N

Susca A

Bacha II

Jinap S

Xu WI

Wang Y

Kong WJ

Subaik M

Luo YB

Huang KL

De Saeger S

MARQUARDT RR FROHLICH AA

Keyword analysis in scientific articles is a point with great interest for exploring and following the many branches of science and engineering [21]. As a result of our study, 5968 different words were retrieved within OTA field during 1965-2016. Figure 10 shows some high-frequency words, which can be roughly classified into four aspects. The largest one is toxin, with mycotoxin and aflatoxin as the top two keywords and the frequency of 1487 and 594, respectively. Second are the common detection methods such as performance liquid chromatography (295), liauid chromatography (254) and immunoaffinity column cleanup (228).

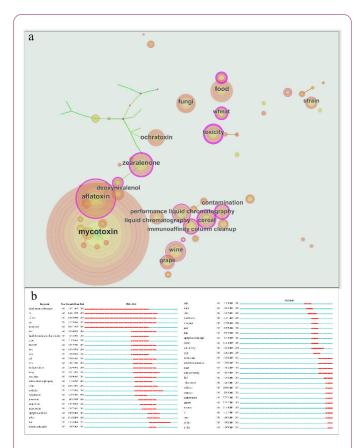


Figure 10 (a) The collaboration patterns of keywords; (b) keywords with burst detection.

In addition, food (372), wheat (217), wine (325), grape (232) and strain (224) can be sorted into one group called the source of OTA. The last one is OTA-related chemical constituents including zearalenone (374) and deoxynivalenol (267). More

 Table 1
 The information about top 20 highest publishing journals.

importantly, toxicity, which is a character of OTA with the frequency number of 291, ranks 10.

The burst detection of 46 keywords is summarised in Figure 10. Three burst times occurred due to nephropathy, Balkan endemic nephropathy and endemic nephropathy with the burst strength of 21.38, 5.12 and 8.04, respectively. Nephropathy, which is one of the main diseases caused by OTA, was the hotspot of concern to research communities before 2004. Currently, aptamer and biosensor, two original detection technologies that can be classified as electrochemistry, have the upper burst strength of 24.78 and 25.15, implying that the new technologies are constantly being developed and possess advantages in OTA detection. Risk assessment related to the subject category of nutrition and dietetics has the strength of 13.20 from 2013 to 2016 owing to the continuous occurrence of poisoning incidents. We infer that it will continue to be the focus of attention because of the increasing awareness of people globally on healthy eating. Moreover, we suggest establishing an exclusive database for OTA, which contains its characteristics, source and biological toxicity and even the analysis of poisoning cases, for the global people. Finally, the world should establish a standard on the maximum OTA in certain food.

Journals and publications

The literature about OTA is from 939 journals. The top 20 productive journals are listed in **Table 1**. Three remarkable journals are the International Journal of Food Microbiology with 175 articles, Food Control with 155 articles and Food Additives and Contaminants with 151 articles, all with more than 150 records. The first two are from the Netherlands; the third one is from the UK. Up to 70% of the journals come from Europe, mainly from the Netherlands (9), Germany (2) and the UK (2). Six journals (30%) are from the USA.

Journal	Number	Percentage %	IF	Region
International journal of food microbiology	175	3.58	3.339	Netherlands
Food control	155	3.17	3.493	Netherlands
Food additives and contaminants	151	3.09	2.047	UK
Food additives and contaminants part a-chemistry analysis control exposure & risk assessment	140	2.86	2.047	UK
Journal of agricultural and food chemistry	136	2.78	3.154	USA
Toxins	113	2.31	3.03	Switzerland
Food and chemical toxicology	108	2.21	3.778	Netherlands
World mycotoxin journal	95	1.94	2.189	Netherlands
Toxicology letters	84	1.72	3.858	Netherlands
Journal of food protection	83	1.7	1.417	USA
Journal of chromatography	70	1.43	3.981	Netherlands
Poultry science	64	1.31	1.908	USA

Journal of aoac international	63	1.29	0.962	USA
Food chemistry	61	1.25	4.529	Netherlands
Analytical and bioanalytical chemistry	56	1.15	3.431	Germany
Toxicology	55	1.12	3.582	Netherlands
Toxicology and applied pharmacology	55	1.12	3.791	Netherlands
Mycopathologia	50	1.02	1.71	Germany
Applied and environmental microbiology	48	0.98	3.807	USA
Journal of the science of food and agriculture	45	0.92	2.463	USA

The higher the impact factor, the greater the breakthrough in the field of OTA. **Table 2** displays the top 18 articles from 10 journals with the highest impact factor. Seven publications (38.9%) were published before 2000. 'OTA in retail flour' was published in The Lancet with an impact factor of 47.83. Three articles were published in Nature before 1975. Five articles were published in Studies in Mycology with an impact factor of 14.00. The paper titled 'Ochratoxin production and taxonomy of the yellow aspergilli (*Aspergillus section circumdati*)', which is the nearest one, was published in 2014 [22-34].

Table 2 Top 10 journals with the highest impact factor.

Rank	Title	Year	Journal	IF	Reference
1	Ochratoxin A in retail flour	1978	Lancet	47.831	[22]
2	Genome sequencing and analysis of the versatile cell factory aspergillus niger	2007	Nature Biotechnology	41.667	[23]
3	Ochratoxin A: a toxic metabolite produced by aspergillus ochraceus wilh;	1965	Nature	40.137	[2,3,24]
	Detection and estimation of ochratoxin A;	1966			
	Relationship of ochratoxin-A to foetal death in laboratory and domestic animals	1971	-		
4	Determination of mycotoxins in human foods	2008	Chemical Society Reviews	38.618	[25]
5	Ochratoxin A may cause testicular cancer	2002	Lancet Oncology	33.9	[26]
6	Molecular aspects of the transport and toxicity of ochratoxin A	2004	Accounts of Chemical Research	20.268	[27]
7	Mycotoxins	2003	Clinical Microbiology Reviews	19.958	[28]
8	Neopetromyces gen. nov and an overview of teleomorphs of aspergillus subgenus circumdati	2000	Studies in Mycology	14	[7,8,29-31]
	Secondary metabolite profiling, growth profiles and other tools for species recognition and important aspergillus mycotoxins	2007	_		
	Biodiversity of aspergillus species in some important agricultural products	2007			
	Diagnostic tools to identify black aspergilli	2007			
	Ochratoxin production and taxonomy of the yellow aspergilli (aspergillus section circumdati)	2014	_		
9	Depletion of intracellular ca2+ stores sensitizes the flow-induced ca2+ influx in rat endothelial cells	2003	Circulation Research	13.965	[32]
10	Combinational o-aryl carbamate and benzamide directed ortho metalation reactions - synthesis of ochratoxin-A and ochratoxin-B;	1985	Journal of the American Chemical Society	13.858	[11,33,34]

The citation score of one article reflects its academic influence in one field. **Table 3** illustrates the top 10 frequently cited references. Up to 80% of them were published before 2000. During our search, the highest locally cited reference is titled 'Risk assessment of the mycotoxin ochratoxin A' with a

total global citation score of 468. The cited frequency of 'OTA: a toxic metabolite produced by *Aspergillus ochraceus Wilh*' published in 1965 is 542. It told the discovery of extracting OTA from *Aspergillus ochraceus Wilh* for the first time [35-42].

Table 3 Top-10 most cited references.

Rank	Title	LCS	GCS	Years	Journal	Reference
1	Risk assessment of the mycotoxin ochratoxin A.	395	468	1989	Biomed Environ Sci	[35]
2	Ochratoxin A: A toxic metabolite produced by Aspergillus ochraceus wilh	377	542	1965	Nature	[2]
3	Cadmium and cadmium compounds, beryllium, cadmium, mercury, and exposures in the glass manufacturing industry	318	335	1993	IARC MON EV CARC RIS	[36]
4	Ochratoxin A in table wine and grape-juice: occurrence and risk assessment	295	355	1996	Food Additives and Contaminants	[37]
5	Ochratoxin A: An overview on toxicity and carcinogenicity in animals and humans	262	429	2007	Molecular Nutrition & Food Research	[38]
6	Determination of ochratoxin-a at the ppt level in human blood, serum, milk and some foodstuffs by high-performance liquid-chromatography with enhanced fluorescence detection and immunoaffinity column cleanup - methodology and swiss data	228	316	1995	Journal of Chromatography B- Biomedical Applications	[39]
7	Mycotoxins	227	1356	2003	Clinical Microbiology Reviews	[28]
8	A review of recent advances in understanding ochratoxicosis	217	282	1992	Journal of Animal Science	[40]
9	Determination of ochratoxin a in wine by means of immunoaffinity column clean-up and high-performance liquid chromatography	196	270	1999	Journal of Chromatography A	[41]
10	Penicillium-viridicatum, Penicillium-verrucosum, and production of ochratoxin-A	185	196	1987	Applied and Environmental Microbiology.	[42]

Conclusion

This paper is expected to reveal fundamental statistics and the hotspots of the scientific activities on OTA. It will benefit scholars in mastering their next research directions to motivate more innovative ideas in this field. Based on our analysis, this field of OTA has entered a stage of high concern. We obtained literature data, which were published from 1965 to 2016, from the WoS database using CiteSpace V and bibliometric methods combined with network analysis. We analyse the data from seven aspects and address three main areas as follows:

Quantity and growth trend of publication numbers

We explored the literature data during 1965–2016 from WoS. A total of 4889 documents about OTA can be searched. All these publications can be divided into three stages. The early stage of steady development occurred during 1965–2010. The number of OTA papers published 2011–2012 fell

sharply with only 33 records in 2012. The year 2013–2016 experienced rapid growth, which can be seen from the amount of 349 published articles in 2016. This trend suggests that the rapid growth is due to aflatoxin contamination in milk and dog food in 2013 throughout Europe and the USA, respectively. However, the mean cited frequency per publication is plummeting from 1966. Only the first paper in 1965 possessed the highest cited frequency with 542. Until 2016, only three were on average. This finding indicates that when the intensity of research is increasing, the quality of articles should be improved at the same time.

Literature analysis at the national level

We mainly displayed the geographic distribution of the most productive and influential countries as well as the international collaboration of each country. Publications are mainly centred in the USA, many European countries and China. The USA ranks the first in North America and also in the world with 543 publications. In Europe, Italy, Germany and

France contributed the majority of articles about OTA. China accounts for 29.94% in Asia with 321 records in the number of articles. We noted that the top three countries with high cited frequencies are Denmark, the Netherlands and Austria, in spite of all of them producing a handful of publications. China published many papers but had less cited frequency. We can conclude that some European countries such as Denmark and France are the most powerful countries on the subject of OTA while the USA has the most articles. However, for many countries (i.e., the top three productive countries), including China, more efforts on OTA are necessary to promote the quality of publications. In addition, the world should establish a standard on the maximum OTA in certain food.

Current hotspots and prospective trends

We implied the current hotspots. According to the analysis of subject frequency, chemistry, toxicology and food science and technology are the main domains explored by scholars. Electrochemistry, nanoscience and nanotechnology and nutrition and dietetics are three emerging subjects with high burst strength and are paid increasing attention. Data suggest that the first two detection methods of OTA are popular along with the science and technology development. Moreover, the third one can be due to people's increasing awareness of healthy eating. We speculate the third one could be a hotspot for a long time in the future. As for keywords, research communities have great interest in two novel and special identification technologies of OTA: aptamer and biosensor. Both technologies have high burst strength, which corresponds to the result of subjects that new identification technologies would attract much attention from scholars in the OTA field next.

The more the publications, the lesser the cited frequencies. Hence, we proposed a hypothesis that with more concerns, wide research and more studies on the field of OTA, research communities would achieve fewer novel breakthroughs and discoveries. The hypothesis could present valuable insights or scientific references for scholars and policymakers. In addition, this paper still includes several limitations:

(1) The data do not involve the nearest literature data in 2017 and the WoS database updates; thus, the results of total publications and citations are not the latest.

(2) The collaboration pattern between different countries and institutions needs to be explored in detail to provide suggestions for promoting OTA research progress.

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