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Aflatoxin – Publication analysis of a global health threat

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ABSTRACT

Background: As a metabolite of *Aspergillus flavus* and *Aspergillus parasiticus*, Aflatoxin is a carcinogenic and mutagenic mycotoxin that is confirmed as a class-1 agent. It contaminates the most of our staple foods, affecting 25% of global crops. It is a global threat to human health by causing liver cancer in conjunction with Hepatitis B. Developing countries are particularly at risk not only because of the climatic but also of the agricultural production conditions. Climatic change and the intensification of global trading are also enhancing the risk of the global contamination. The overall health effects are dramatic.
Methods: Therefore, we choose this mycotoxin for an in-depth analysis of its global scientific publication output. The focus is on the geographical and chronological facts and trends, the international networks and the development of research fields. For this purpose, the bibliometric data was collected in the Web of Science database and interpreted according to a variety of scientometric parameters.
Results: The results show a superiority of the USA regarding the absolute publication numbers that was taken over by China in 2016. Not only the dramatic incidence and prevalence rates of liver cancer and the high Aflatoxin contamination rate in China, but also the immense increase of the expenditure for research and development play a role.
In relation to the integration of socio-economic features other countries emerge, i.e. Tunesia, Nigeria or Egypt. Other severely affected countries of Africa, Asia and South-America show a relatively low publication output. India, as an emerging country, achieves a considerably high output. Here, the health hazards are threatening and resulted in an outbreak of Aflatoxicosis induced Hepatitis in 1974. Although an outbreak of Aflatoxicosis in Kenya caused the deaths of 120 people, Kenyan research output is relatively low. The analyses of the distribution over time in 5-year intervals showed the relative decrease of the research area *Oncology*, whereas *Food Science & Technology* gained proportionally importance.
Conclusions: For future Aflatoxin studies, it is extremely important to carry out projects with the participation of the most affected countries and to support and enhance the knowledge growth of the individual farmers to establish more adapted production practices.

1. Introduction

Foodborne diseases remain a tremendous global challenge. Hence, promoting food safety is an important key to protect human life and health. According to the World Health Organization (WHO), an estimated 600 million people are affected by foodborne illnesses each year leading to the necessity to improve global food safety by multidisciplinary actions on local, national and international levels. Globalization and the intensified trade of agricultural commodities (Schaffartzik et al., 2014) in conjunction with a changing climate cause unique challenges and health hazards that have to be addressed immediately, not only in the developing countries but also in the industrial world (Frazzoli, Gherardi, Saxena, Belluzzi, & Mantovani, 2016).

The FAO (Food and Agriculture Organization of the United Nations) estimates that approximately 25% of the crops are infested by mycotoxins (FAO, 2017). Moldy contamination plus warm and humid conditions facilitated by global warming are prerequisites for the production of Aflatoxins – the toxic metabolites of *Aspergillus*

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flavus and *Aspergillus parasiticus* (Medina, Rodriguez, & Magan, 2014). These fungi are natural contaminants of food such as cereals, nuts, vegetables, fruits, spices and meat. Aflatoxins are invisible, odor- and tasteless. They affect foods at every stage of their production. The infestation before harvest is relatively difficult to eliminate, whereas contamination after harvest can be controlled by rapid drying and clean storage practices (Medina et al., 2014). In farm animals, Aflatoxin ingestion impacts growth and the immune system, which strains local meat production, national economy and the global food supply (Wild & Gong, 2010).

Aflatoxins affect human health in numerous ways. The IARC (International Agency for Research on Cancer) classified the fungal metabolites as class-1 agents. Aflatoxins are cancerogenic, particularly in conjunction with a chronic Hepatitis B virus (HBV) infection. The causal relationship with Hepatitis C virus seems probable but is not strongly proved (Wild & Montesano, 2009). Aflatoxins are linked to a statistically significant risk for Hepatocellular Carcinoma (HCC) (Qian et al., 1994; Ross et al., 1992). The WHO reported 788,000 global deaths due to HCC in 2015 and ranked the condition as the second common cause of cancer death – following lung cancer – worldwide (WHO, 2017). In the developing world, the two risk factors for HCC – HBV and Aflatoxin – are highly prevalent (Liu & Wu, 2010). This finding might explain why HCC occurs mainly in less developed countries; here, 83% of new cases have been registered in 2012 (WHO, 2012). Furthermore, Aflatoxicosis (Wild & Gong, 2010) due to acute Aflatoxin poisoning can be life threatening; common symptoms include digestion problems, severe edema, haemorrhage, and acute liver damage. Chronic exposition is accompanied with dysfunctional digestion and growth retardation as well as fetal congenital malformations in pregnant women (Sarma, Bhetaria, Devi, & Varma, 2017). Many countries reacted with strict legal Aflatoxin limits regarding a variety of foods. In 2006, the European Commission set the maximum Aflatoxin B1 level (AFB1) at 2.0 μg/kg in grain or grain products and at 0.1 μg/kg for processed cereal based baby foods (European Commission, 2006). In the United States of America (USA), higher levels of AFB1 (20 μg/kg) are tolerated by the Food and Drug Administration (FDA). The agency decided on 0.5 μg/kg as a maximum level of Aflatoxin M1 (AFM1) in milk (FDA, 2000).

Strict regulations on trading practices, food monitoring and storage methods have been implemented in the industrialized world and led to successfully reduce the Aflatoxin related health risks (Brown, Chen, Cleveland, & Russin, 1999). Inhabitants of developing or underdeveloped countries remain particularly vulnerable for malnutrition from food borne diseases and suffer from the lack of resources, knowledge and technology. In 2006, a survey showed that more than 5 billion people were exposed to the intake of contaminated food in developing countries (Sarma et al., 2017; Strosnider et al., 2006). Rural populations are mainly at risk due to the persisting subsistence production (Plymoth, Viviani, & Hainaut, 2009; Strosnider et al., 2006). Also, an occupational hazard exists for various employees such as farm workers who experience an airborne ingestion due to contaminated stables or animal feed (IARC, 2017) amongst other injuries (Bhattarai et al., 2016) (Moen, Kayumba, Sakwari, Mamuya, & Bratveit, 2016; Schneberger, Aulakh, Channabasappa, & Singh, 2016). Next to occupational exposure, Aflatoxin in food or the feed chain is the most hazardous threat to human health. Here, the mycotoxin exposure varies considerably due to the source, the type of food, the kind of storage and the climatic conditions (Sanders, Blankenship, Cole, & Hill, 1984). Especially the consumption of maize, cereals, peanuts and milk – via the feed-food carry over has to be seen critically. Whereas these commodities are staples of the modern and globalized world, they are responsible for the human exposure to high Aflatoxin levels (Wild & Gong, 2010).

Aflatoxins and the related foodborne diseases constitute a global problem and a major Public health challenge. This translates into a necessity to increase awareness among food producers, handlers and consumers as well as authorities to minimize Aflatoxin exposure – particularly in the developing countries. On national and international level, regulatory policies need to be customized to ensure a safe consumer environment. To address these needs, further research and the implementation of related public health measures are important future steps. To plan scientific endeavors and the distribution of financial support, the scientific output on „Aflatoxin“ needs to be evaluated. Therefore, this particular topic was selected for the *New Quality and Quantity Indices in Science* (NewQIS) project (Groneberg-Kloft, Quarcoo & Scutaru, 2009) presented here. We performed a scientometric analysis to quantify related research output and to evaluate the scientific productivity of single countries within the framework of the international research landscape.

2. Methods

2.1. Methodological platform

The multidisciplinary NewQIS platform was founded in 2009 by specialist in the fields of engineering, computer sciences and medicine (Groneberg-Kloft et al., 2009). The authors published a standardized and validated methodology, which was used to conduct studies on numerous relevant topics (Groneberg, Braun, Klingelhoefer, Bundschuh, & Gerber, 2016; Groneberg, Geier, et al., 2016; Quarcoo, Bruggmann, Klingelhofer, & Groneberg, 2015; Schreiber, Klingelhofer, Groneberg, & Bruggmann, 2016). Aims of NewQIS include the (1) objective, precise and reliable scientometric analysis of the global research publication output, which is evaluated chronologically and geographically, (2) the depiction of the results in global maps based on density equalizing map projections (DEMP), and (3) the investigation of national and international scientific collaborations. These transparent data allow researchers, decision makers and funding institutions to evaluate the present global research landscape related to "Aflatoxin", to plan research endeavors and to allocate research funds according to identified shortcomings.

2.2. Data source

The online database "Web of Science Core Collection (WoS)" from Thomson Reuters (by now *Clarivate Analytics*) was used to identify and retrieve the articles on Aflatoxin. WoS is one of the most comprehensive and renowned sources for scientific publications. The platform provides numerous relevant bibliometric data and facilitates the quantification of citations via its unique *Citation Report* function. The data for the socio-economic analyses has been extracted from the World-Factbook (CIA, 2015).

2.3. Search procedure and data integration

The term (*aflatoxin*) was used to search in the title, the author's key words and the abstract. The evaluation period was set from January 1st, 1900 until December 31st, 2016. All document types were involved. The biomedical context was ensured by filtering the subject categories. Afterwards, the bibliometric data was stored as plain text files, and processed as a data base file in order to serve as information source for the envisaged analyses.

2.4. Data analyses

The bibliometric data was evaluated regarding the publication languages, the document types as well as the chronological and geographical aspects. A special focus has been set on high profile articles and their relevance for the scientific settings. Additionally, a novel graphical animation of the publication development over time has been generated. The countries' research outputs were not only quantified in absolute numbers but were also analyzed in terms of associated citation rates and socio-economic features (R_{POP} = number of articles/population in mill. inhabitants; R_{GDP} = number of articles/Gross Domestic Product in 1000 bn US-Dollars). The international networks as well as the collaborating partners have been evaluated and depicted. The analyses of the subject areas and the assigned author's keywords represent other main issues of the present study.

2.5. Illustration of findings

For visualization, cartograms were generated according to the density equalizing map projection method (DEMP). This technique was developed and published by Gastner and Newman (Gastner & Newman, 2004). Herewith, a distortion of the world map – that follows the physical osmotic flow principle – increases or reduces the size of the countries according to specific parameter of interest. In this study, the absolute figures of articles and citations as well as citation rate and socio-economic ratios have been visualized by means of DEMP.

The findings of the keyword analyses have been visualized inter alia with the VOS Viewer software (VOSviewer, 2017).

3. Results

In total, 5122 articles (n) directly related to Aflatoxin were retrieved from the WoS database. Out of this data pool, 5019 articles were written in English (nearly 98%). Other publications languages were French, German, and Spanish with two digit numbers. Less than 10 publications were written in Russian, Japanese, Chinese, Portuguese, Dutch, Malay or Polish. Looking at the document type, 92.5% (n = 4741) were journal articles, 5.9% (n = 301) were published as proceedings papers and 1.5% (n = 79) as book chapters. One article was listed as a retracted publication.

3.1. Chronological analyses

Although the health problems related to Aflatoxin contamination have a much longer history, the WoS indexed the first related article in 1963. Afterwards, the annual number of Aflatoxin publications rose steadily but remained under 100 per year until the 1990s. Then, additional features were introduced in the WoS allowing the user to search not only in the title but also in the abstract, respectively the author's keyword. This improvement in the search ability was followed by a slight increase in the annual number of publications that dropped under 100 published items in 2007 again. Afterwards, a continuing increase reached an annual number of 252 publications in 2016 (Fig. 1A).

The number of citations (c) per year paralleled the chronological development of the annual publication output over time. In 1990, approximately 1000 citations related to "Aflatoxin" publications per year were reached. This number increased steeply to more than 5000 in 1991. The highest number was reached in 1996 with c = 6,716, only to drop again up to now. We documented other citation peaks in 2001 (c = 5519) and 2002 (c = 5480) (Fig. 1B).

The ten most prolific articles regarding their citation numbers were collected and compiled in Table 1.

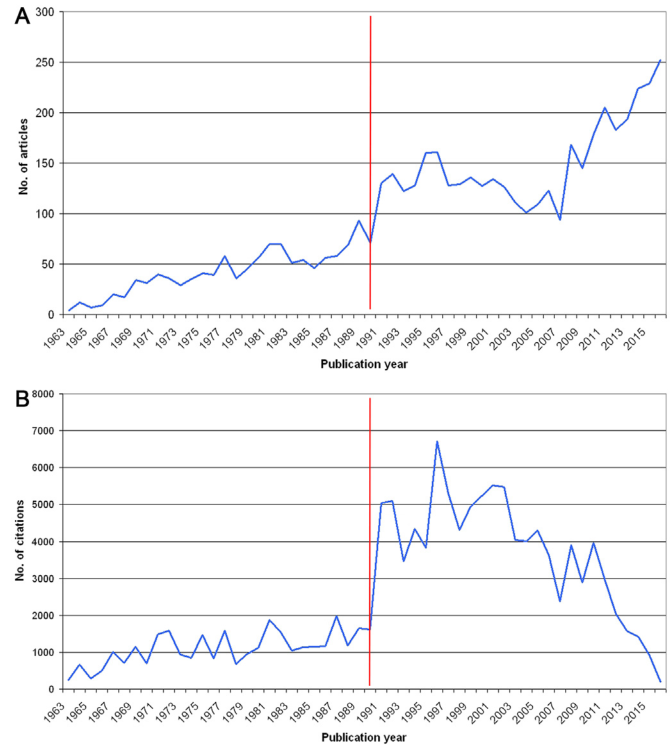

Fig. 1. Analyses over time (1963–2016). A) No. of publications. B) No. of citations. Red Line: Introduction of the Topic-search in WoS and the associated inclusion of abstracts and author's keywords in the search. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.2. Geographical analyses

112 countries, respectively autonomous regions participated in the publication of the examined Aflatoxin articles. Out of the whole database, 4895 articles (95.5%) could be associated with one or more country of origin. The first year that delivered the address information of a representative quantity of articles was 1973, so that the evaluation period of all geographical and collaboration analyzes was set from 1973 until 2016.

3.3. Country analyses

The USA published the highest number of articles (n = 1759) in the period under review, followed by China (n = 372), the United Kingdom (UK) with n = 362, India (n = 296), and France (n = 289) as the five most productive countries (Fig. 2A). More so, the USA had the highest number of citations (c = 57,434). Second ranked was the UK (c = 12,330), followed by China (c = 9413), France (c = 8462) and Japan on the 5th position (c = 8248).

Regarding the citation rate (CR), the Switzerland is the country (threshold ≥ n = 30) with the highest value (CR = 45.41), followed by Austria (CR = 40.16), Taiwan (CR = 38.31), Finland (CR = 36.82) and the UK (34.06) (Fig. 2 B).

Since these numbers represent the average value of the evaluation period from 1973 to 2016, it is reasonable to take a look at the development over time (Video 1). In 1973, only 10 countries published on Aflatoxin with the USA as the country publishing the highest number of articles. While the absolute number of articles increased in the course of time (Fig. 1A), the order of the countries with the highest productivity in the field following the USA varied. In 1975, India appeared among them for the first time. It was also striking that African countries such as Nigeria and Kenya published

Table 1
The 10 most cited articles.

Author	Year	Citations	Title
Shimada, T. et al., USA, Japan	1996	646	Activation of chemically diverse procarcinogens by human cytochrome P-450 1B1
Creppy, E.E., France	2002	508	Update of survey, regulation and toxic effects of mycotoxins in Europe
Hoult, J.R.S., Paya, M., United Kingdom	1996	499	Pharmacological and biochemical actions of simple coumarins: Natural products with therapeutic potential
Harris, C.C., USA	1991	497	Chemical and physical carcinogenesis - advances and perspectives for the 1990s
Newberne, P.M., Butler, W.H., USA	1969	476	Acute and chronic effects of aflatoxin on liver of domestic and laboratory animals
Ross, R.K. et al., China, USA	1992	467	Urinary aflatoxin biomarkers and risk of hepatocellular-carcinoma
Lunn, R.M. et al., USA, Taiwan	1999	455	XRCC1 polymorphisms: Effects on aflatoxin B-1-DNA adducts and glycophorin A variant frequency
Garner, R.C. et al., USA	1972	441	Liver microsomal metabolism of aflatoxin-B1 to a reactive derivate toxic to salmonella-typhimurium TA-1530
Qian, G.S. et al., USA, China	1994	440	A follow-up-study of urinary markers of aflatoxin exposure and liver-cancer risk in shanghai
Hustert, E. et al., Germany, USA	2001	423	The genetic determinants of the CYP3A5 polymorphism

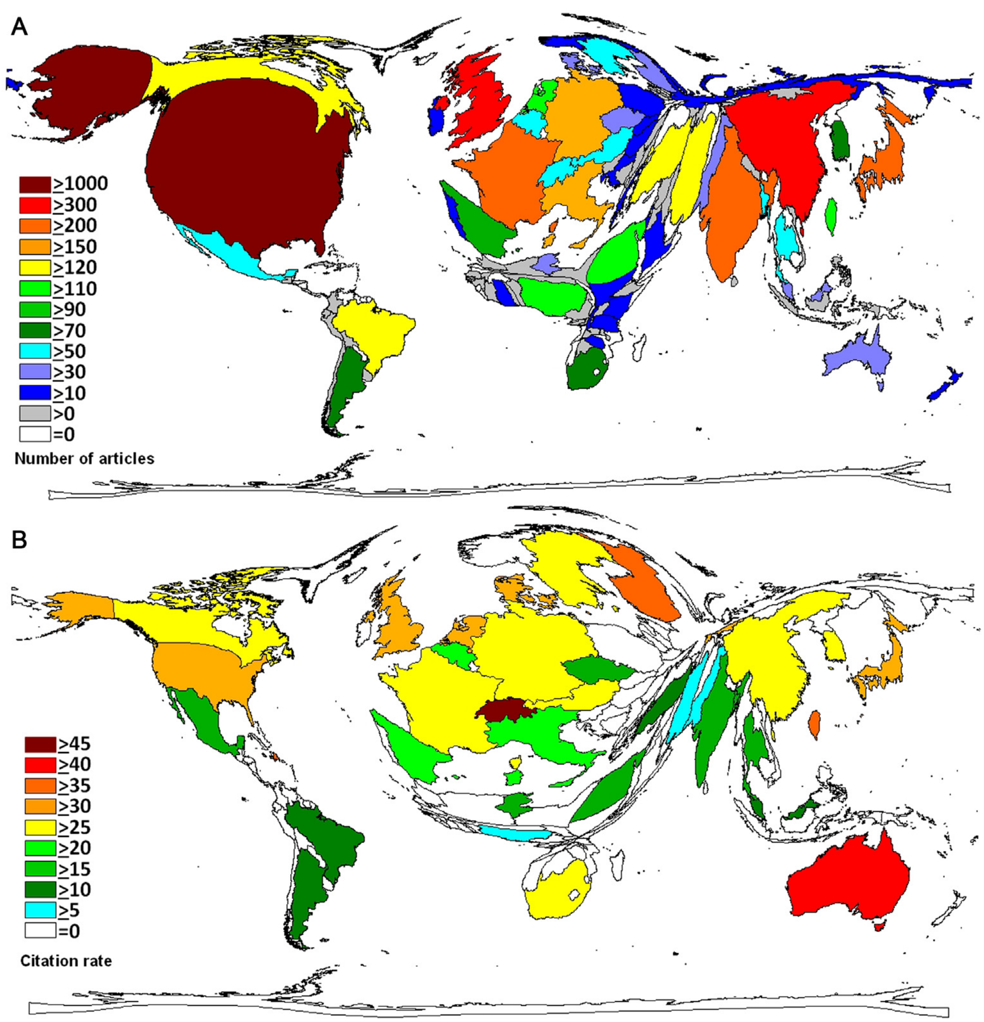

Fig. 2. Density equalizing map of the country's publication performance. A) Absolute number of articles. B) Average citation rate (threshold ≥ 30 articles).

on Aflatoxin in the 1970s. Nigeria was the first African country interested in this topic with 8 articles (11th position). For the first time, the USA lost their rank as most publishing country to China in 2014. So, the global picture has changed considerably in 2016. Fifty-eight different countries worked on Aflatoxin, among which China published the most articles (n = 50), followed by the USA (n = 46), Iran (n = 19), Italy (n = 14) and Spain (n = 13). Among the European countries that had a stable position over time, the UK and France fell back in the ranking. The first African country publishing on Aflatoxin was Nigeria with 8 articles on the 11th position.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.foodcont.2018.02.017.

Due to the enormous differences regarding the economic power and the number of inhabitants of the publishing countries, we additionally carried analyses of the number of articles in relation to socio-economic parameters (GDP in 1000 bn USD = Gross Domestic Product in 1000 billion US-Dollar, population numbers) and evaluated them according to their World Bank categories. Here, again another global picture could be drawn (Fig. 3). The findings emphasised the position of Tunisia as a Low-Middle Income country (LMI) regarding the ratio of the number of articles/GDP in 1000 bn USD (R_{GDP}) that reached a value of $R_{GDP} = 305.81$) as well as the ratio of the number of articles/inhabitants in mill. (R_{POP}) with $R_{POP} = 3.59$). Other LMI countries, Nigeria and Egypt, reached front positions with their R_{POP} ratios. Otherwise, European High-Income countries (HI) lead the list (Table 2): Austria ($R_{GDP} = 163.5$, $R_{POP} = 7.81$), Finland ($R_{GDP} = 163.04$, $R_{POP} = 7.09$), Denmark ($R_{GDP} = 147.28$, $R_{POP} = 6.97$), Belgium ($R_{GDP} = 133.70$, $R_{POP} = 5.96$), the Netherlands ($R_{GDP} = 131.65$, $R_{POP} = 6.70$), and the UK ($R_{GDP} = 129.84$, $R_{POP} = 5.62$).

3.4. Collaboration analyses

In total, only 956 articles (19.6%) were the outcome of bi- or multilateral collaborations. Only from 1990 onwards, the number of collaboration articles per year rose to two-digital figures. As of this date, the annual number of collaborative publications increased continuously until 2015. 2015 represents the most productive year until now, 77 articles were authored within international collaborations (Fig. 4A).

Authors with affiliations to two countries published 752 articles out of the 956 collaborative items; 147 articles involved three partnering countries. The number of cooperatively produced articles decreased with an increasing number of participating countries (Fig. 4B). The highest number of 15 collaborating countries was reached in the workgroup report “Public health strategies for reducing Aflatoxin exposure in developing countries” by H. Strosnider et al. from 2006 (Strosnider et al., 2006). The Center of Disease Control and Prevention in Atlanta USA (CDC) and the World Health Organization, Switzerland (WHO) established this workgroup in July 2005 after the outbreak of acute Aflatoxicosis in Kenya that caused significant morbidity (317 cases) and mortality (125 deaths) (Lewis et al., 2005).

3.5. Research areas

The database includes articles from 76 different subject areas (WoS categories). The most assigned area with n = 2567 articles was *Toxicology*, followed by *Oncology* (n = 925) and *Food Science & Technology* (n = 916). Other much assigned fields were: *Pharmacology & Pharmacy* (n = 717), *Genetics & Heredity* (n = 447), *Public, Environmental & Occupational Health* (n = 353) and *Nutrition & Dietetics* (n = 309).

Considering the distribution in the most publishing countries (Fig. 5B), differences could be shown. Comparatively, Brazil (0.9%), Turkey (1.0%) and Iran (2.8%) published relatively very little in the field of *Oncology*. By contrast, the contribution of Turkey and Iran was proportionally higher in the field of *Food Science & Technology* (Turkey = 12.4%, Iran = 15.6%). In Japan, *Public, Environmental & Occupational Medicine*, with approximately 0.8%, was hardly assigned, whereas it was much stronger in the field of *Genetics & Heredity* (16.8%). Iran and Turkey published above average in *Public, Environmental & Occupational Medicine* with 15.6% and 12.4% respectively.

The analysis of author's keywords showed six main thematic clusters. Distinctions can be made between AFB1 (grains etc.) and AFM1 (milk), as well as their impact on HCC and medical implications. Other clusters are related to the various contaminated

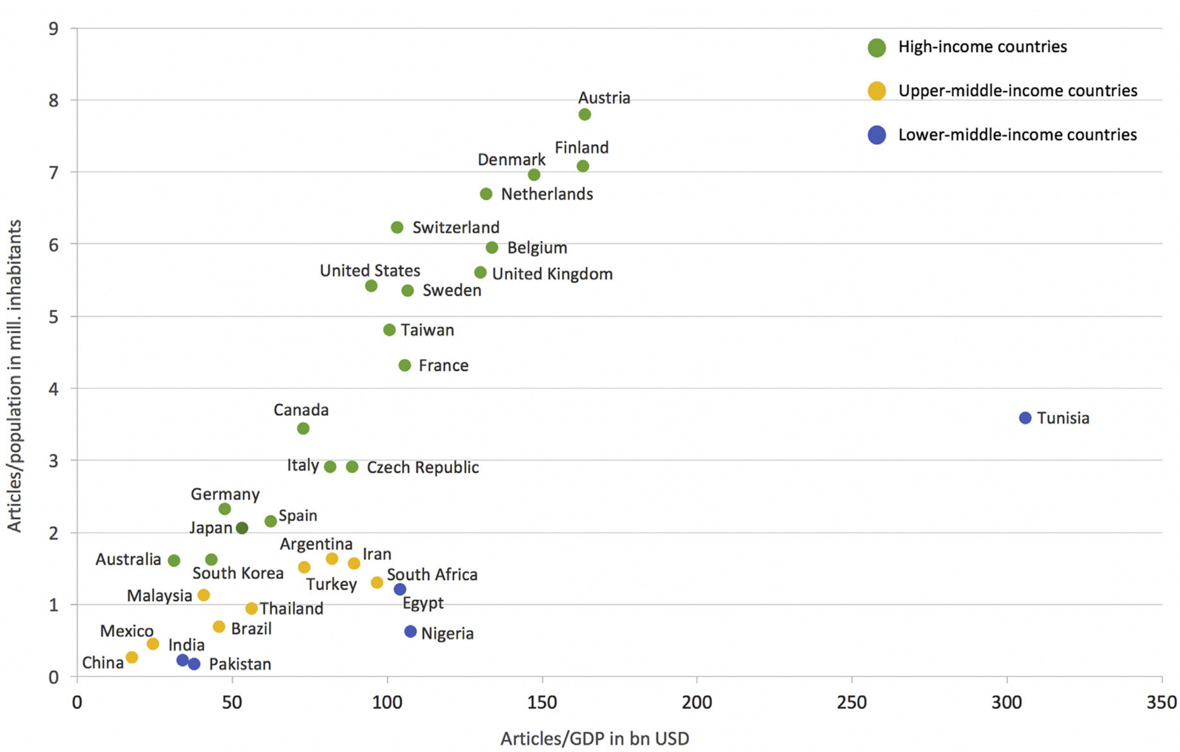

Fig. 3. Socio-economic country analysis. The data for the socio-economic analyses has been extracted from the World-Factbook (CIA, 2015).

Table 2
The chronological development of the country's publication performance (1973–2016).

Country	No. of articles	GDP (bn USD)	Articles/GDP (1000 bn USD)	Rank	Population (mill.)	Articles/Population (mill.)	Rank
Tunisia	40	130.8	305.81	LMI1	11.13	3.59	LMI1
Austria	68	415.9	163.50	HI1	8.71	7.81	HI1
Finland	39	239.2	163.04	HI2	5.50	7.09	HI2
Denmark	39	264.8	147.28	HI3	5.59	6.97	HI3
Belgium	68	508.6	133.70	HI4	11.41	5.96	HI6
Netherlands	114	865.9	131.65	HI5	17.02	6.70	HI4
United Kingdom	362	2788	129.84	HI6	64.43	5.62	HI7
Nigeria	117	1089	107.44	LMI2	186.05	0.63	LMI3
Sweden	53	498.1	106.40	HI7	9.88	5.36	HI9
France	289	2737	105.59	HI8	66.84	4.32	HI11
Egypt	115	1105	104.07	LMI3	94.67	1.21	LMI2
Switzerland	51	494.3	103.18	HI9	8.18	6.24	HI5
Taiwan	113	1125	100.44	HI10	23.46	4.82	HI10
South Africa	71	736,3	96.43	UMI1	54.30	1.31	UMI4
United States	1759	18560	94.77	HI11	324.00	5.43	HI8
Iran	130	1459	89.10	UMI2	82.80	1.57	UMI2
Czech Republic	31	350.9	88.34	HI12	10.64	2.91	HI14
Argentina	72	879.4	81.87	UMI3	43.89	1.64	UMI1
Italy	181	2221	81.49	HI13	62.01	2.92	HI13
Turkey	122	1670	73.05	UMI4	80.27	1.52	UMI3
Canada	122	1674	72.88	HI14	35.36	3.45	HI12
Spain	105	1690	62.13	HI15	48.56	2.16	HI16
Thailand	65	1161	55.99	UMI5	68.20	0.95	UMI6
Japan	261	4932	52.92	HI16	126.70	2.06	HI17
Germany	188	3979	47.25	HI17	80.72	2.33	HI15
Brazil	143	3135	45.61	UMI6	205.82	0.69	UMI7
South Korea	83	1929	43.03	HI18	50.92	1.63	HI18
Malaysia	35	863.8	40.52	UMI7	30.95	1.13	UMI5
Pakistan	37	988.2	37.44	LMI4	202.00	0.18	LMI5
India	296	8721	33.94	LMI5	1266.88	0.23	LMI4
Australia	37	1189	31.12	HI19	22.99	1.61	HI19
Mexico	56	2307	24.27	UMI8	123.17	0.45	UMI8
China	372	21270	17.49	UMI9	1373.54	0.27	UMI9

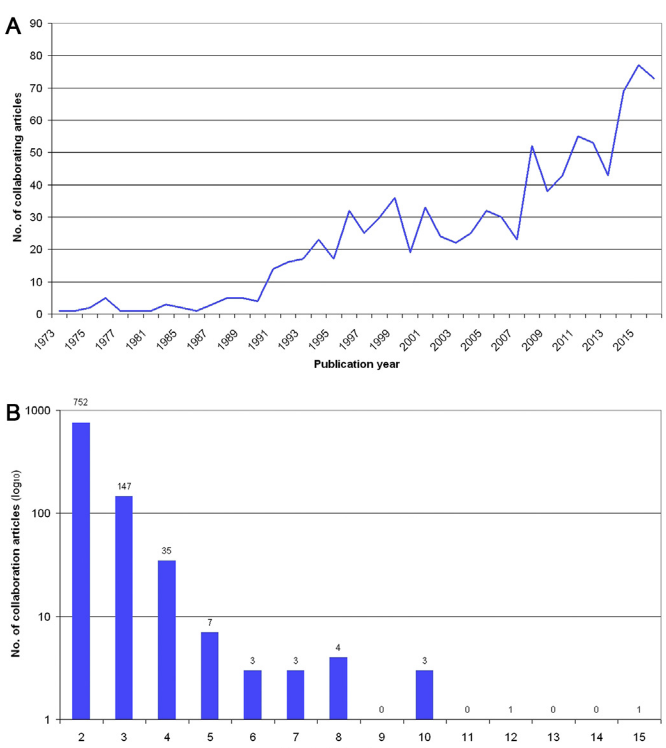

Fig. 4. International collaborations. A) Development over time (1973–2016). B) No. of partner countries (logarithmic display).

products, the exposure assessment and the various types of mycotoxins (Fig. 6).

4. Discussion

4.1. Development over time

Our analysis identified 5122 Aflatoxin-related articles that were listed in the WoS from 1963 to 2016. The first article described Aflatoxin B1 in contaminated peanut flour. The authors were B.H. Armbrecht et al. (Armbrecht, Smith, Nelson, & Hodges, 1963), who discovered this mycotoxin type in England for the first time. Since 1963 the number of articles related to Aflatoxin increased steadily each year, which parallels the overall growing scientific output in the biomedical field during the last 150 years (Van Noorden, 2014). This development can be attributed to the innovation of technology and publication procedures, but also to the modified publication activity and behavior of authors. The necessity for scientists to publish in order to gain recognition and receive funding based on their productivity is discussed globally, even in its negative ways (Angell, 1986).

In our study, the substantial increase of the annual publication numbers in 1990/1991 (indicated by the red line in Fig. 1) can be explained by a methodological reason. The WoS developed the "Topic search" by then, which allows the user to extend the search to abstract and keywords leading to the identification of more publications related to a specific topic. Nevertheless, regional outbreaks of Aflatoxicosis sparked an intensified scientific interest noticeable a short time later. Especially, some affected countries raised their research efforts significantly (Chap. 3.2).

Our study could document an association between important

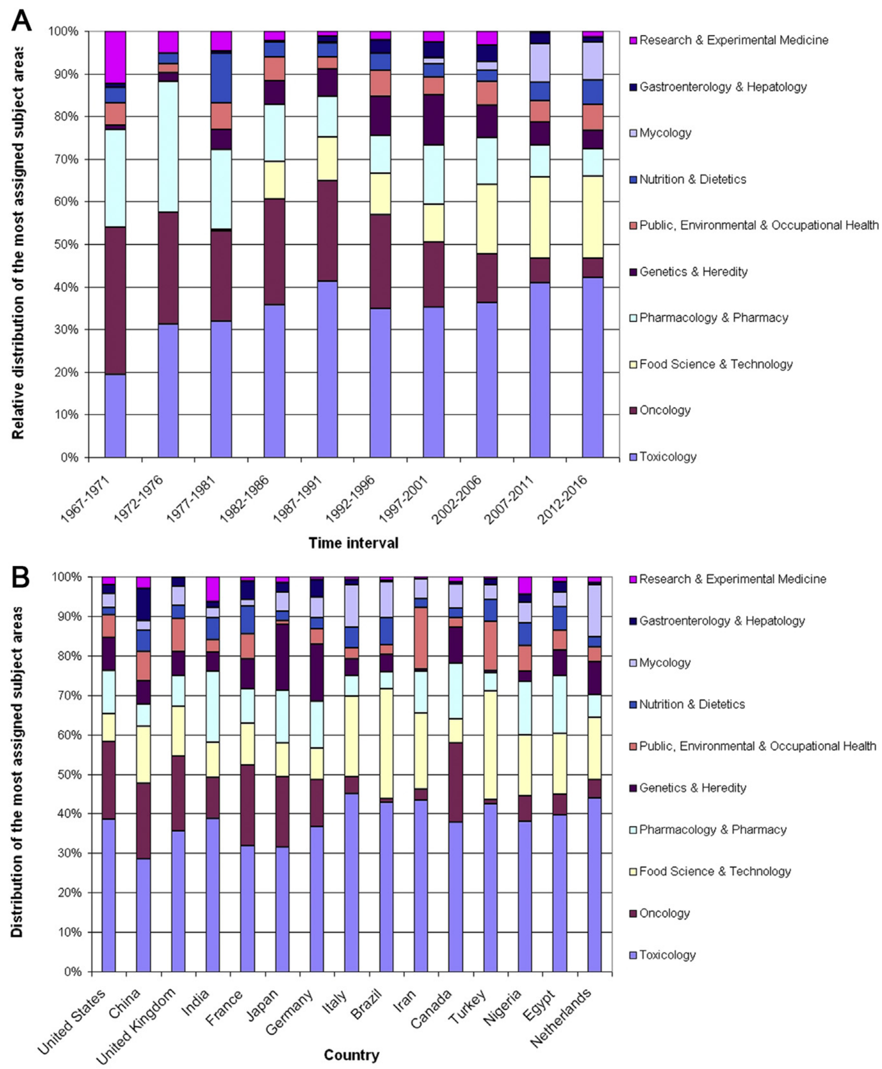

Fig. 5. Subject areas. A) Relative distribution of the most assigned subject areas in 5-year intervals (1967–2016). B) Relative distribution of the most assigned subject areas in the most publishing countries.

milestones in Aflatoxin research and the publication of high-impact research in the field. In 1996, two of the most recognized articles related to Aflatoxin have been published (Table 1). The US-Japanese collaboration article "Activation of chemically diverse procarcinogens by human cytochrome P-450 1B1" by T. Shimada et al. (Shimada et al., 1996) received c = 646 citations. In this study, it was excluded that cytochrome P-450 produces a genotoxic product from Aflatoxin B1. Also published in 1996, the British review "Pharmacological and biochemical actions of simple coumarins: Natural products with therapeutic potential" by J.R.S. Hoult and M. Paya (Hoult & Paya, 1996) got c = 499 citations as third most cited paper of this study. As Aflatoxins are based on the coumarin structure, they were analyzed in terms of their therapeutic potential as anticoagulants, which was found to be rather limited. In 2002, the second most cited article has been published (c = 508) by E.E. Creepy (France) (Creppy, 2002). It is a review on the survey, regulation and toxic effects of mycotoxins in Europe. The last two items we mentioned can be classified as reviews, although they were indexed as articles by the WoS, which explains why they were included in the study.

We observed a decrease in citation numbers after 2010, which can be explained by the *Cited Half Life* (CHL) phenomenon described by Eugene Garfield (Garfield, 2007). The CHL of biomedical articles is seven to eight years (Martin-Martin, E, JM, & ED, 2015). This time is needed to obtain half of the overall citations of a publication. Hence, younger publications need more time to reach their citation maximum leading to an increase in the citation numbers in the coming years.

4.2. *Publication landscape and geographical development*

The landscape of the worldwide publication output on Aflatoxin follows a global research effort distribution similar to other relevant biomedical topics as shown in previous bibliometric analyses (Bruggmann et al., 2017; Groneberg, Braun, et al., 2016). The strong position of the USA and European countries can be attributed to the high expenditures these respective nations dedicate to Research and Development (R&D). The outstanding research productivity of these nations reflects the excellent scientific infrastructure the local research communities can benefit from. Also, North-American and European scientists are able to utilize long standing and extremely prolific national and international networks, which have been established in a majority of research areas.

Besides the comparison of the absolute publication numbers

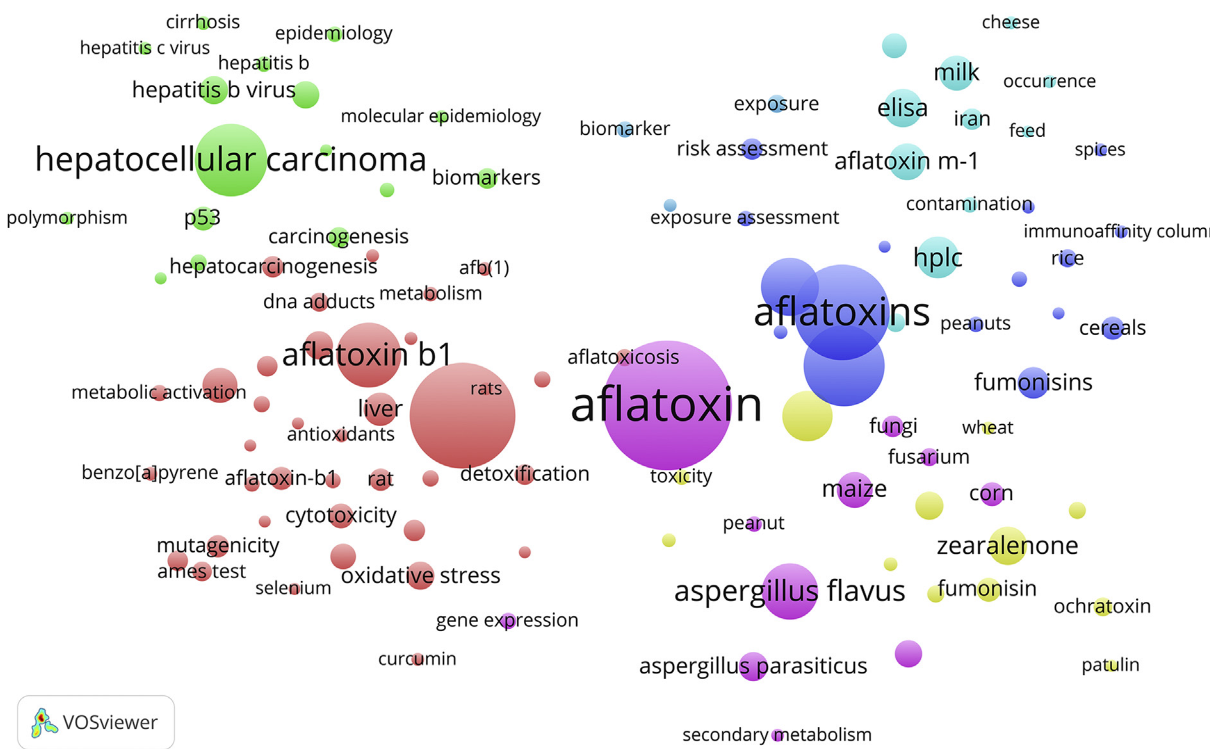

Fig. 6. Clusters of author's keywords, visualized with the VOSviewer software.

throughout the whole evaluation period, China and India show a comparatively high output. The description of the geographic development of Aflatoxin research in this study underpins the growing effort these countries made in this field. This finding is unique to Aflatoxin research since it could not be shown in other bibliometric analyses, and can be explained by specific epidemiological and cultural reasons (Bruggmann et al., 2017; Gotting, Schwarzer, Gerber, Klingelhofer, & Groneberg, 2017). In spite of the decrease of the prevalence of HBsAg (Hepatitis-B-virus surface antigen, indicating an active infection) in China from 10% in 1992 to 7% in 2006, it is still high according to the definition of the WHO in 2016. With one-third of the Hepatitis-B infections worldwide, the Chinese Hepatitis rate is the highest in the world. In 2015, 93 mill. people were infected, among which were 20 mill. patients with chronic Hepatitis B (Chinese Society of Hepatology, 2015; WHO, 2016). In 2012, the WHO estimated that 50% of the new liver cancer cases occurred in China alone (WHO, 2012). Here, more than 300,000 people are dying each year from hepatocellular carcinoma (Chinese Society of Organ Transplantation, 2014). Additionally, recent studies still show a wide Aflatoxin contamination of Chinese staple foods (Gao et al., 2011; Wu et al., 2016). Hence, Chinese authorities seem to have responded to the apparent problems and made Aflatoxin research a high and growing priority in China. Further in addition to the epidemiological and ecological reasons, China has been increasing the overall expenditures for R&D, and reduced the gap to the EU already in 2012. Also, the country is expected to overtake the USA in the near future (OECD, 2014). The findings of this study emphasize this connection. The correlation between the countries' number of articles and their expenditure in R&D is significant with Spearman $r2 = 0{,}9029$ ($p < 0{,}0001$).

As an emerging country, India was ranked high regarding its Aflatoxin research. It is the world's largest producer of dairy products and has the largest dairy animal population. Rastogi, Dwivedi, Khanna, and Das (2004) found AFM1 contamination in 87.3% of infant milk products and milk samples, and Reddy, Reddy, & Muralidharan (2009) detected AFB1 up to 308 μg/kg in 67.8% of the collected rice samples. In 2006, the government of India passed a law called the *Food Safety and Standards Act* (Frazzoli et al., 2016). An outbreak of Hepatitis in Western-India associated with the intake of heavily Aflatoxin contaminated maize occurred in 1974 (Krishnamachari, Nagarajan, Bhat, & Tilak, 1975), causing a sharp rise of number of Indian publications in 1975. Since the mid-1980s India was contributing relatively steadily to the global Aflatoxin publications.

Astonishingly, Nigeria was among the most productive countries publishing on Aflatoxin. In contrast to other NewQIS studies (Groneberg, Geier, et al., 2016; Quarcoo et al., 2015), the majority of the Nigerian publications were issued by local scientists and not in cooperation with researchers from other countries. Here, the expansion of Nigeria's economy - a country that recently surpassed even South Africa as the leading African nation - has certainly to be taken into account. Thereby, Nigeria can expend substantial R&D specific funds to facilitate research targeting Aflatoxin and related issues.

As a LMI country, Tunisia stands out regarding the socio-economic analyses, especially their R_{GDP} value is clearly upfront. Tunisian authors wrote more than 50% of their articles in collaboration, mainly with French scientists. As a former colony, stable economic and scientific ties have been developed that led to an institutional setup keeping up with the global performance. Ghali et al. (Ghali, Hmaissia-Khlifa, Ghorbel, Maaroufi, & Hedili, 2008) found an Aflatoxin contamination in 50.5% of the most consumed commodities in Tunisia. Contaminations in a not inconsiderable extent could also be detected in sorghum and pistachios (Ghali et al., 2009). Otherwise, the findings of the socio-economic analyses showed also a distinct privilege of the HI countries, especially the European countries to fund Aflatoxin research. Publishing UMI countries were placed in the midfield. In contrast to the absolute numbers, here China and India were thrown back. Their huge number of inhabitants caused a lower ranking in the R_{POP} analysis. Also, their comparable higher GDP affected them adversely.

Overall, it can be concluded that China, India, Nigeria and Tunisian established an infrastructure that allows scientists to perform research in a relevant field aiming to successfully address and alleviate a real burden of the local population. In contrast, other countries with Aflatoxicosis or Hepatitis outbreaks occurring in the past were positioned lower among the most publishing countries, i.e. Kenya was placed only on rank 38, Malaysia on rank 32, and Thailand reached rank 23. Nevertheless, a population based study in Kenya produced the most recognized article, and has been carried out in collaboration with the Tropical Products Institute in London (UK) in 1973 (Peers & Linsell, 1973). The Kenyan collaboration with the USA (CDC) on the Aflatoxicosis outbreak in 2005 ranked second (Lewis et al., 2005). In Malaysia, 13 children died during an acute Hepatic Encephalopathy outbreak due to Aflatoxins in 1988 (Lye, Ghazali, Mohan, Alwin, & Nair, 1995). The most cited article from Thailand was a case control study in collaboration with Canada. It is dealing with liver-cancer (Parkin et al., 1991), but no association with Aflatoxin intake could be found. Although Aflatoxin levels in Nepal and Bangladesh are comparable to the contamination levels that caused the Kenyan outbreak, no visible scientific productivity could be detected for these nations in WoS (Lye et al., 1995).

4.3. Development of research areas

When research fields were analyzed, we showed that the medical publications are mainly focused on the carcinogenic impact of long-term Aflatoxin exposure (Williams et al., 2004). The subject categories *Toxicology* and *Oncology* were the most assigned areas. Also, the keyword cluster built around the term "Hepatocellular Carcinoma" constitutes a very prominent group.

However, the share of publications that were assigned to *Oncology* decreased considerably over time. The subject area *Food Science and Technology* first appeared in 1982 and was assigned with increasingly higher numbers afterwards. This finding can be explained by the growing importance of food safety facilitated by improved production conditions that shifted in the focus of the scientific studies. This finding underlines the global concern of the health consequences related to Aflatoxin contaminated food. Even if the high risks are present in developing countries, the thread is coming closer to the industrial world facilitated by global trading and the climatic change.

4.4. Methodological limitations

With respect to limitations of the applied methodology, we acknowledge that all studies, which are based on data collection provided by online databases, are depending on the quality of the used database. The WoS Core Collection database offers bibliometric and citation data of relevant publications that are reviewed by a peer review process ensuring a high scientific quality. Until now, the WoS displays a preference for English journals and has an English bias, so that the dominance of English-speaking nations within the scientific community dedicated to Aflatoxin research can be partially explained. In this respect, we also acknowledge that it is not possible to identify and analyze every article ever published worldwide – particularly the non-English ones – published on Aflatoxin so far. The requirements to get indexed in the WoS are high and leading to a preselection of scientific literature that has to be further discussed too. Comparably, non-English literature is cited less frequently leading to a disadvantage of non-English journals (Garfield, 2001). Also, fast developing fields receive an advantage over unyielding topics (Della Sala & Crawford, 2007). Nevertheless, the utilization of the WoS as data source for our study seemed to be the best – and above all the most valuable – choice since the integrated *Journal Citation Report* allows the analysis of the citation numbers and all listed entries fulfil strict minimum requirements. Other data sources that provide the citation numbers are limited regarding the covered time span (*Scopus*) or the accuracy of citations (*Google Scholar*) (Kulkarni, Aziz, Shams, & Busse, 2009). Insofar, the findings may be considered as representative, valuable and meaningful despite some methodical limitations.

5. Conclusions

Until now, the human exposure of Aflatoxin can be controlled by regulations and expensive production processes in the industrialized world. In developing countries, these possibilities are not a matter of course so the respective health threats are still enormous. In this context, the data of a recent IFPRI study (*International Food Policy Research Institute*, USA) can be expected. The study deals with the chronic malnutrition of children caused by damage of the colon. This condition might be determined prenatally and attributed to the consumption of Aflatoxin contaminated food during pregnancy (Hoffmann, Jones, & Leroy, 2015; Kruchem, 2016). The findings of this study will certainly set new benchmarks not only for the Aflatoxin research but also for governmental decisions and the focus of development aid.

In this study, we could identify many productive nations dedicated to Aflatoxin research. Others that are greatly affected by this particular related Public Health burden are not visible among the most productive countries in the field. In terms of these shortcoming, it should be called for the involvement of the most affected but less productive countries within collaborative networks to foster science in a mutual way. Their individual needs and requirements as well as their limited access to cost-intensive research, production methods or high development costs should have maximum priority for decision makers, funders and scientists all over the world.

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List of abbreviations

AF	Aflatoxin
CDC	The Center of Disease Control and Prevention
CR	Citation rate
FAO	Food and Agriculture Organization
FDA	Food and Drug Administration
GDP	Gross domestic product
HBsAg	Hepatitis-B-virus surface antigen
HBV	Hepatitis B virus
HCC	Hepatocellular Carcinomas
HI	High-income country
IARC	International Agency for Research on Cancer
IFPRI	International Food Policy Research Institute
JIF	Journal impact factor
LMI	Low-middle-income country
NewQIS	New Quality and Quantity Indices in Science
R_{GDP}	Ratio of no. of articles/GDP in 1000 bn USD
R_{POP}	Ratio of no. of articles/population in mill
R&D	Research & Development
UK	United Kingdom
UMI	Upper-middle-income country

USA United States of America
USD US-Dollar
WHO World Health Organization
WoS Web of Science

Declaration section

Ethics approval and consent to participate: N/A.

Consent for publication: N/A.

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Author's contribution: DK, DAG contributed to conception, design and analyses. DK, YZ collected the data. DK, YZ, MB, MHKB, DB, DAG contributed to the interpretation of data. DK drafts the article. DK, YZ, MB, MHKB, DB, DAG revised the article. DK, YZ, MB, MHKB, DB, DAG have participated in the final approve of the manuscript.

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