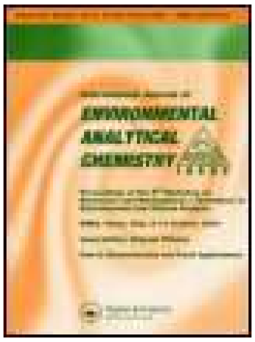

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Prevalence and concentration of ochratoxin a in spices: a global systematic review and meta-analysis study

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ABSTRACT
Ochratoxin A (OTA) is one of the most important toxic metabolites of fungi found in agricultural products. This study aimed to estimate the prevalence and concentration of OTA in spices through meta-analysis. Therefore, online databases including PubMed, Embase, Web of Science, and Scopus were screened systematically from 1995 to 2022 to collect the related data. After assessing eligibility, 36 articles with 1686 samples were included in the current study. According to the findings, the global pooled prevalence of OTA was counted as 50% (95% CI: 47–52%). Also, a positive correlation between the prevalence of OTA with the year of study, region, and sample size was observed. Moreover, the highest and lowest concentrations of OTA in spices were noted in paprika (50.66 ng/g) and cinnamon (3.4 ng/g), respectively. The outcome of this meta-analysis can be used for risk assessment model development, aiming to help the government and industries to find a specific way to reduce the prevalence of OTA spice products.

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KEYWORDS
Ochratoxin A; spice; meta-analysis; prevalence; concentration

1. Introduction

Spices are generally derived from the non-leafy parts of the source plants including the seeds, bark, root, flowers, or fruits [1]]. They are widely used to enhance aroma, taste, colour, smell, and flavour in daily food preparations [2]. Due to their preservative characteristics, spices have potential applications in the food industry. On the other hand, these products are among the most efficient plant species for medical purposes because of their treatment effects on acute and chronic diseases. In this context, spices are rich sources of various phytochemicals [3]. Phytochemicals are a large group of bioactive compounds found in plants that have potential protective effects on the health of humans [3,4]. These natural compounds consists of flavonoids and other phenolic chemicals, thus provide protection against oxidation by reacting with free radicals or forming complexes with metal ions. For

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example, several antioxidants from spices, such as gingerol (ginger), eugenol (red pepper), and curcumin (turmeric), coumarin (cumin), were experimentally evidenced to control cellular oxidative stress due to render antioxidant activity and their ability to scavenge free radicals [5]. Besides, antimicrobial, antidiabetic, and immunomodulatory effects of some spices have been confirmed, such as cinnamon. In addition, curcumin is a spice compound and able to act as an anti-inflammatory agent by interacting with various inflammatory processes [6]. Spices can contribute to the prevention and treatment of some cancers due to their anti-oxidative characteristics [7]. In terms of trade value, red chilli, black pepper, paprika, turmeric, cumin, coriander, cumin, nutmeg, and ginger are the most important spices used all over the world [8]. Spice crops are cultivated in different geographic areas, but most of them originated in India (74%), Bangladesh (6%), Turkey (5%) and China (5%) [9]. In recent years, there have been increasing concerns over the food safety of consumers. Several factors including poor harvesting practices, improper storage, processing, packaging, drying method, and distribution influence fungal growth responsible for spoilage and mycotoxin production [10]. All the steps during production and storage have critical effects on spice quality. Fungal contamination of spices is one of the main issues that may occur at all the steps during production and storage and is very important from human health perspective. Fungal contamination of spices leads to serious consequences for animal and human health by the production of mycotoxins [11]. Mycotoxins are a limited group of toxic secondary metabolites, mainly synthesised by some fungal species belong to the genera Aspergillus, Penicillium, and Fusarium [12,13]. To date, over 400 mycotoxins have been identified among these metabolites, OTA is one of them and can contaminate a wide range of agricultural commodities including cereal, coffee, cocoa, nuts, and spices under certain environmental conditions [14,15]. Ochratoxin A (OTA) is the most studied mycotoxin in spices that its prevalence depends on many specific factors and among them, temperature, storage conditions, and processing are the most described factors. Humans are exposed to this metabolite through consumption of contaminated food products [16]. Exposure to this mycotoxin is a life-threatening problem and can have many toxicological effects on consumers. OTA intake through the consumption of contaminated crops can cause some adverse effects such as kidney and liver diseases, as well can target the nervous system, and immune system in test animals [17–19]. In addition, this molecule has been classified as a possible human carcinogen (group 2B) by the International Agency for Research on Cancer (IARC) [20]. To avoid such outcomes, processing protocols and storing conditions must be controlled to obtain a good quality product [21]. However, given the health risks of exposure to OTA, regulatory agencies or commissions, have imposed national standards on its contamination in agricultural products, which may vary in different countries. For instance, the European Commission has established levels up to 15 ng/g for OTA in the spices [22]. Meta-analysis refers to the statistical analysis of collected data from multiple independent studies in order to investigate the integration of results.

To the best of our knowledge, no systematic reviews have been conducted to assess the prevalence and concentration of OTA in spices; however, some assessments were carried out to measure the mycotoxin levels in different food commodities. Therefore, due to the lack of global systematic review, the current investigation aimed to estimate the prevalence and concentration of OTA in various spices (pepper, paprika, chilli, cinnamon, turmeric, nutmeg, ginger, cayenne, and curry) via a systematic review and meta-analysis approach.

2. Materials and method

2.1. Search strategy

A systematic literature search was carried out to investigate the prevalence and concentration of OTA in spices. In this regard, relevant articles were collected from international databases including PubMed, Scopus, Embase, and Web of Science between 1995 to January 2022. Search keywords used included spice; mycotoxins; and OTA. Besides, the references list of all articles was also screened in order to collect other suitable studies.

3. Inclusion or exclusion of criteria

After first screening by the title and abstract, the eligible articles were obtained. Two authors read and cheeked the screened articles based on the following research criteria independently.

Each author reviewed the titles, abstracts, and full texts of the papers to select the articles with the inclusion criteria, and any differences were resolved by dispute and consensus. The inclusion criteria were: (1) Full-text available; (2) reporting prevalence and/or concentration data of OTA; (3) only spice samples; (4) cross-sectional research; studies conducted from 1995 to January 2022; only published in the English language. Additionally, the following items were adopted as exclusion criteria: (1) Books, theses, and review articles; (2) OTA contamination in other agricultural products; (3) any other mycotoxins prevalence.

4. Data extraction

The data were extracted by one of the authors and checked by another author. All the required data such as first author, publication year, country, total sample size, type of spice, number of positive samples, the prevalence of OTA, the mean and standard deviation of OTA, the limit of detection (LOD), and limit of quantification (LOQ) were included in the Microsoft Excel software (Microsoft Corporation, WA, US).

5. Meta-analysis and meta-regression of data

In the present study, the random effect model (REM) was used to estimate the pooled concentrations and prevalence of OTA in spices with 95% confidence intervals for all evaluated articles. This test was also applied to calculate the overall prevalence in subgroups such as country, continent, and type of spice products. The heterogeneity of data was determined by Chi-square (I^2) index and Cochrane Q test with $P < 0.05$. The range of the I^2 index was between 0 and 100%, and when I^2 index ≥50 values indicate that considered heterogeneous. Meta-regression was used to determine the effects of sample size, year, and country on the prevalence of OTA in spices using the method of moment model [23]. Publication bias among the included studies was detected statistically by using Egger's test [24]. As publication bias among studies was significant (P-value < 0.05), the Meta Trim test was performed to estimate the pooled prevalence of OTA in the spices to eliminate the publication bias [25]. All data were analysed using STATA 14.0 (2015; STATA 14.0 Statistical Software, College Station, TX, USA). Statistical difference was significant at $p < 0.05$.

6. Results

6.1. Study selection

The flow diagram of the systematic search in Scopus, PubMed, Embase, and Web of Science databases is outlined in the PRISMA diagram (Figure 1). After the removal of duplicates ($n = 635$) a total of 490 articles were obtained for further investigation. Considering the titles and abstracts, 402 that did not meet our inclusion criteria were excluded. Full texts of 88 remaining articles were assessed and based on the eligibility criteria 36 articles with 65 studies were included in the current meta-analysis.

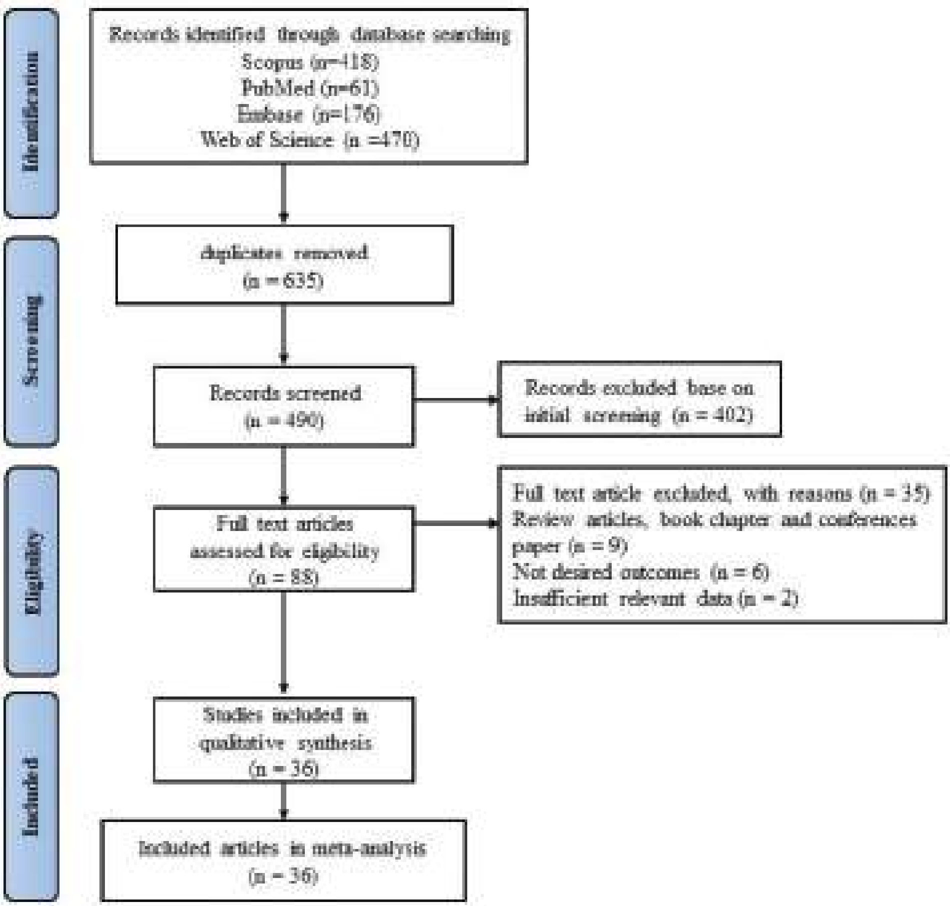

Figure 1. Flow chart for studies selection process.

7. Study characteristics

The main characteristics of the included studies are displayed in Table 1. According to the methods used for detection and quantification, the presence of OTA was determined by HPLC, TLC, LC-MS/MS, enzyme-linked immunosorbent assay (ELISA) and UHPLC. Eleven studies were conducted in Asia [26,33–35,40,43,45,51,52,54,61], sixteen in Europe [27–30,36–38,46,48,50,53,55–58,60], six in Africa [31,41,42,44,47,59], and three in America [32,39,49]. These studies were published between 1995 and 2020. The selected articles reported OTA prevalence data in different countries globally. Among all studies 20 (30.3%) studies were related to black pepper; 14 (21.2%) studies were paprika; 8 (12.1%) studies were cinnamon; 7 (10.6%) studies were turmeric; 8 (12.1%) studies were ginger; 9 (13.6%) studies were red pepper. The data from black pepper, paprika, turmeric, ginger, and red pepper was entered to the present study. As shown in Table 1 the prevalence of OTA contamination in the included studies ranged from 0 to 100 for spices. Totally, collected data from 1686 spice samples were pooled for this meta-analysis.

8. Meta-analysis

8.1. Prevalence of OTA

The overall prevalence of OTA in spices was 50% (95% CI: 47–52%) (Figure 2). The prevalence of OTA in the black pepper, paprika, cinnamon, turmeric, ginger, and red pepper was 31% (95% CI: 14–51%), 73% (95% CI: 44–95%), 15% (95% CI: 0–42%), 50% (95%CI: 16–84%), 29% (95% CI: 15–45%) and 42% (95% CI: 14–72%), respectively (Figure 3). The rank order of spices based on prevalence of OTA was paprika (73%) > turmeric (50%) > red pepper (42%) > black pepper (31%) > ginger (29%) > cinnamon (15%). Furthermore, based on locations the highest prevalence of OTA in spices was noticed in Netherland 100% (95% CI: 29–100%) and the lowest prevalence rate was in Serbia 0% (95% CI: 0–0.08%) (Table 2). Moreover, the rank of countries regarding the occurrence of OTA in spices was ordered as Netherland > Czech Republic = Canada > Spain > Poland > Tunisia > Malaysia > Côte d'Ivoire > India > Iran > Nigeria > Turkey > Hungary > Italy > Brazil > Russia > South Africa > Cameroon > China > Belgium > Egypt > Latvia > Serbia.

Results also declared that considering the OTA prevalence in spices based on continents, the maximum level was found in America, 58% (95% CI: 19–92%). Also, prevalence rates of 41% (95% CI: 26–57%) and 37% (95% CI: 19–58%) were observed in Asia and Europe, respectively (Table 3). Given the continent prevalence of OTA in spices, Africa showed the lowest value of 36% (95% CI: 21–53%).

9. Concentration of OTA

The rank order of spices based on the mean concentration of OTA was paprika (50.66) > black pepper (30.57) > turmeric (24.29) > ginger (17.13) > red pepper (4.94) > cinnamon (3.4). The overall concentration of OTA in spices was 24.51 ng/g. The highest concentration of OTA in black pepper was noticed in Tunisia (274 ng/g); paprika in Tunisia (203 ng/g); turmeric in India (125.9 ng/g); ginger in India (82.8 ng/

Table 1. Main characteristics of included studies.

Author (year)	Country	Continent	Type of spice	Sample size	Positive	Prevalence (%)	Concentration mean (ng/g)	Method of detection	Reference
Jalili et al. (2015)	Iran	Asia	Black pepper	20	8	40	1.5	HPLC	[26]
Yogendrarajah et al. (2013)	Belgium	Europe	Black pepper	10	1	10	48	HPLC – MS/MS	[27]
Santos et al. (2010)	Spain	Europe	Paprika	64	63	98		HPLC	[28]
Waśkiewicz et al. (2013)	Poland	Europe	Black pepper	5	4	80	9.46	LC/MS/MS	[29]
Waśkiewicz et al. (2013)	Poland	Europe	Cinnamon	4	3	75	2.14	LC/MS/MS	[29]
Waśkiewicz et al. (2013)	Poland	Europe	Turmeric	1	1	100	11.72	LC/MS/MS	[29]
Hierro et al. (2008)	Spain	Europe	Paprika	21	14	67	11.9	HPLC-MS	[30]
Zaied et al. (2010)	Tunisia	Africa	Black pepper	20	13	65	274	HPLC	[31]
Zaied et al. (2010)	Tunisia	Africa	Paprika	23	15	70	203	HPLC	[31]
Kolakowski et al. (2016)	Canada	America	Paprika	100	100	100	149	HPLC	[32]
Kolakowski et al. (2016)	Canada	America	Turmeric	100	90	90	1.92	HPLC	[32]
Jeswal et al. (2015)	India	Asia	Black pepper	42	33	78.5	154.1	ELISA	[33]
Jeswal et al. (2015)	India	Asia	Turmeric	35	20	57.1	125.9	ELISA	[33]
Jeswal et al. (2015)	India	Asia	Ginger	36	20	55.5	82.8	ELISA	[33]
Zareshahrabadi et al. (2020)	Iran	Asia	Turmeric	20	2	10	1.07	HPLC	[34]
Zareshahrabadi et al. (2020)	Iran	Asia	Red pepper	20	11	55	1.52	HPLC	[34]
Zareshahrabadi et al. (2020)	Iran	Asia	Black pepper	20	20	100	49.29	HPLC	[34]
Zareshahrabadi et al. (2020)	Iran	Asia	Cinnamon	20	15	75	18.5	HPLC	[34]
Cao et al. (2013)	China	Asia	Ginger	20	6	30		UPLC-FLR	[35]
Darra et al. (2019)	Italy	Europe	Black pepper	4	1	25	2.3	LC-MS/MS	[36]
Darra et al. (2019)	Italy	Europe	Paprika	3	2	66.66	11.4	LC-MS/MS	[36]
Darra et al. (2019)	Italy	Europe	Turmeric	2	1	50	2.4	LC-MS/MS	[36]
Darra et al. (2019)	Italy	Europe	Cinnamon	3	0	0	0	LC-MS/MS	[36]
Darra et al. (2019)	Italy	Europe	Ginger	3	0	0	0	LC-MS/MS	[36]
El-Kady et al. (1995)	Egypt	Europe	Black pepper	5	0	0		TLC	[37]
El-Kady et al. (1995)	Egypt	Europe	Red pepper	5	0	0		TLC	[37]
Fazekas et al. (2005)	Hungary	Europe	Red pepper	70	32	45.7		HPLC	[38]
Fazekas et al. (2005)	Hungary	Europe	Black pepper	6	0	0	0	HPLC	[38]
Garcia et al. (2018)	Brazil	America	Cinnamon	13	0	0	0	HPLC	[39]
Garcia et al. (2018)	Brazil	America	Black pepper	15	0	0	0	HPLC	[39]
Jalili et al. (2010)	Malaysia	Asia	Black pepper	30	17	56.7	2.167	HPLC	[40]
Lippolis et al. (2017)	Nigeria	Africa	Ginger	89	33	37	2.76	HPLC	[41]
Manda et al. (2016)	Côte d'Ivoire	Africa	Ginger	30	15	50	0.12	HPLC	[42]
Salari et al. (2012)	Iran	Asia	Red pepper	36	6	17		TLC	[43]
Motloung et al. (2018)	South Africa	Africa	Paprika	7	1	14	11	LC-MS/MS	[44]
Ozbey et al. (2012)	Turkey	Asia	Black pepper	23	4	17.4	1.82	HPLC-FD	[45]
Ozbey et al. (2012)	Turkey	Asia	Cinnamon	17	0	0	0	HPLC-FD	[45]

(*Continued*)

Table 1. (Continued).

Author (year)	Country	Continent	Type of spice	Sample size	Positive	Prevalence (%)	Concentration mean (ng/g)	Method of detection	Reference
Boonzaaijer et al. (2008)	Netherland	Europe	Paprika	3	3	100	4.5	LC-MS/MS	[46]
Nguegwouo et al. (2018)	Cameroon	Africa	Black pepper	20	2	10	3.30	ELISA	[47]
Santos et al. (2011)	Spain	Europe	Paprika	17	17	100		HPLC	[48]
Santos et al. (2011)	Spain	Europe	Paprika	4	4	100		HPLC	[48]
Shundo et al. (2009)	Brazil	America	Paprika	70	60	85.7	7	HPLC-FLD	[49]
Skarkova et al. (2013)	Czech Republic	Europe	Red pepper	12	12	100	19	HPLC-FD	[50]
Skarkova et al. (2013)	Czech Republic	Europe	Black pepper	12	11	92	0.83	HPLC-FD	[50]
Thirumala-Devi et al. (2001)	India	Asia	Black pepper	26	14	53.84		ELISA	[51]
Thirumala-Devi et al. (2001)	India	Asia	Ginger	25	2	8		ELISA	[51]
Thirumala-Devi et al. (2001)	India	Asia	Turmeric	25	9	36		ELISA	[51]
Tosun et al. (2016)	Turkey	Asia	Red pepper	75	71	94.7	3.5	HPLC-FLD	[52]
Yogendrarajah et al. (2014)	Belgium	Europe	Black pepper	82	7	8.53	30.9	UPLC	[53]
Zhao et al. (2014)	China	Asia	Cinnamon	80	4	5	1.1	HPLC-FLD	[54]
Goryacheva et al. (2007)	Russia	Europe	Paprika	6	2	33		ELISA	[55]
Goryacheva et al. (2007)	Russia	Europe	Red pepper	7	3	43		ELISA	[55]
Goryacheva et al. (2007)	Russia	Europe	Black pepper	5	0	0		ELISA	[55]
Goryacheva et al. (2007)	Russia	Europe	Ginger	5	0	0		ELISA	[55]
Molnár et al. (2018)	Hungary	Europe	Paprika	53	21	39.6		HPLC	[56]
Reinholds et al. (2017)	Latvia	Europe	Paprika	50	2	4	7.5	UHPLC	[57]
Škrbić et al. (2013)	Serbia	Europe	Red pepper	13	0	0		UHPLC	[58]
Škrbić et al. (2013)	Serbia	Europe	Black pepper	2	0	0		UHPLC	[58]
Aziz et al. (1998)	Egypt	Africa	Ginger	5	2	40		TLC	[59]
Aziz et al. (1998)	Egypt	Africa	Cinnamon	5	0	0		TLC	[59]
Reinholds et al. (2016)	Latvia	Europe	Black pepper	50	0	0		HPLC	[60]
Jalili et al. (2016)	Iran	Asia	Black pepper	23	10	43.5	3.31	HPLC	[61]
Jalili et al. (2016)	Iran	Asia	Red pepper	23	4	17.4	5.66	HPLC	[61]
Jalili et al. (2016)	Iran	Asia	Turmeric	23	7	30.4	2.77	HPLC	[61]
Jalili et al. (2016)	Iran	Asia	Cinnamon	23	8	3.5	5.46	HPLC	[61]

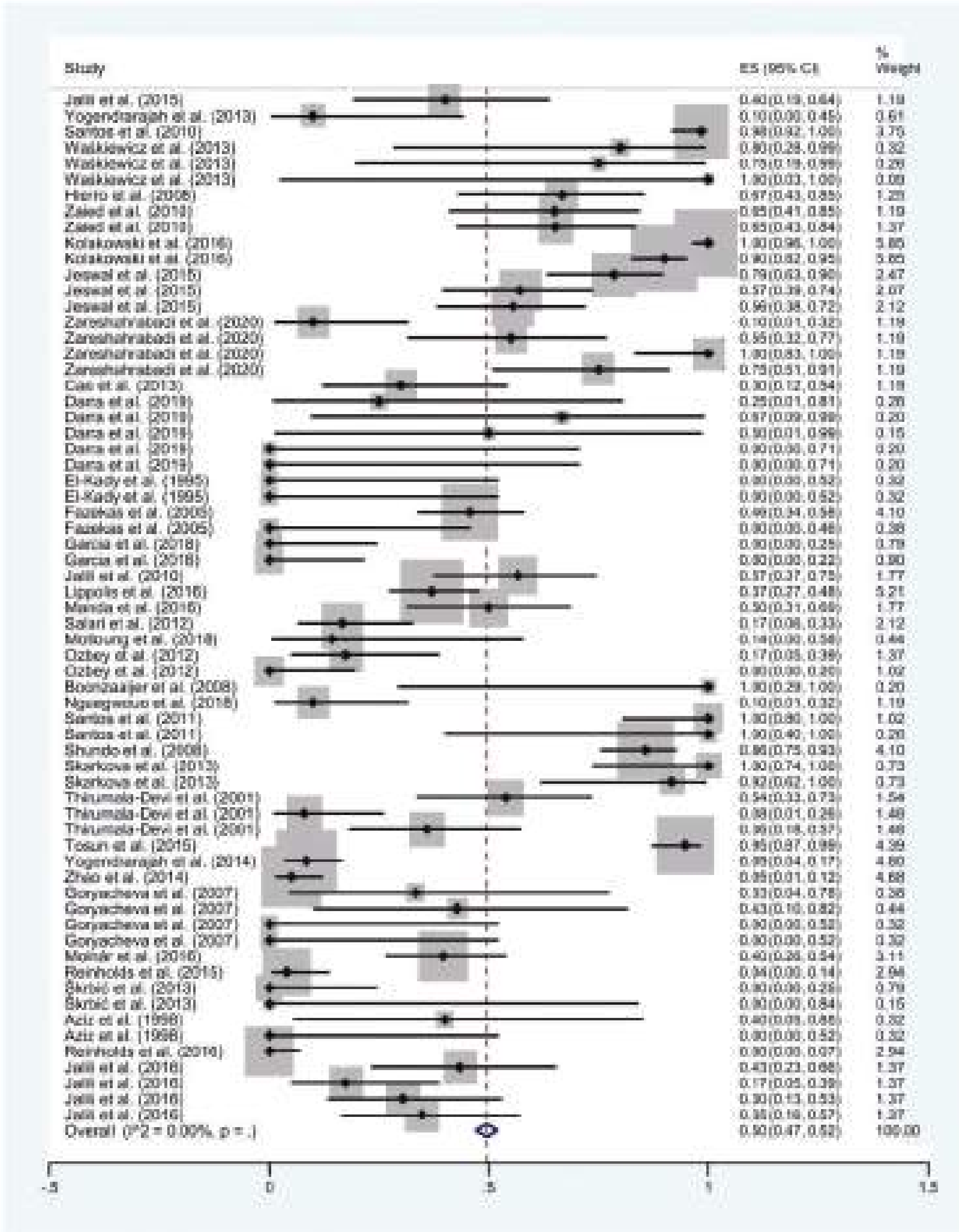

Figure 2. Forest plots for random-effects meta-analysis of prevalence of OTA in the spice samples. Effect size (ES) is prevalence of OTA in any study.

g); red pepper in Czech Republic (19 ng/g); and cinnamon in Iran (18.5 ng/g) (Table 4). In addition, Asia (32.68 ng/g) and Europe (13.22 ng/g) had a higher and lower concentrations of this compound, respectively (Table 5).

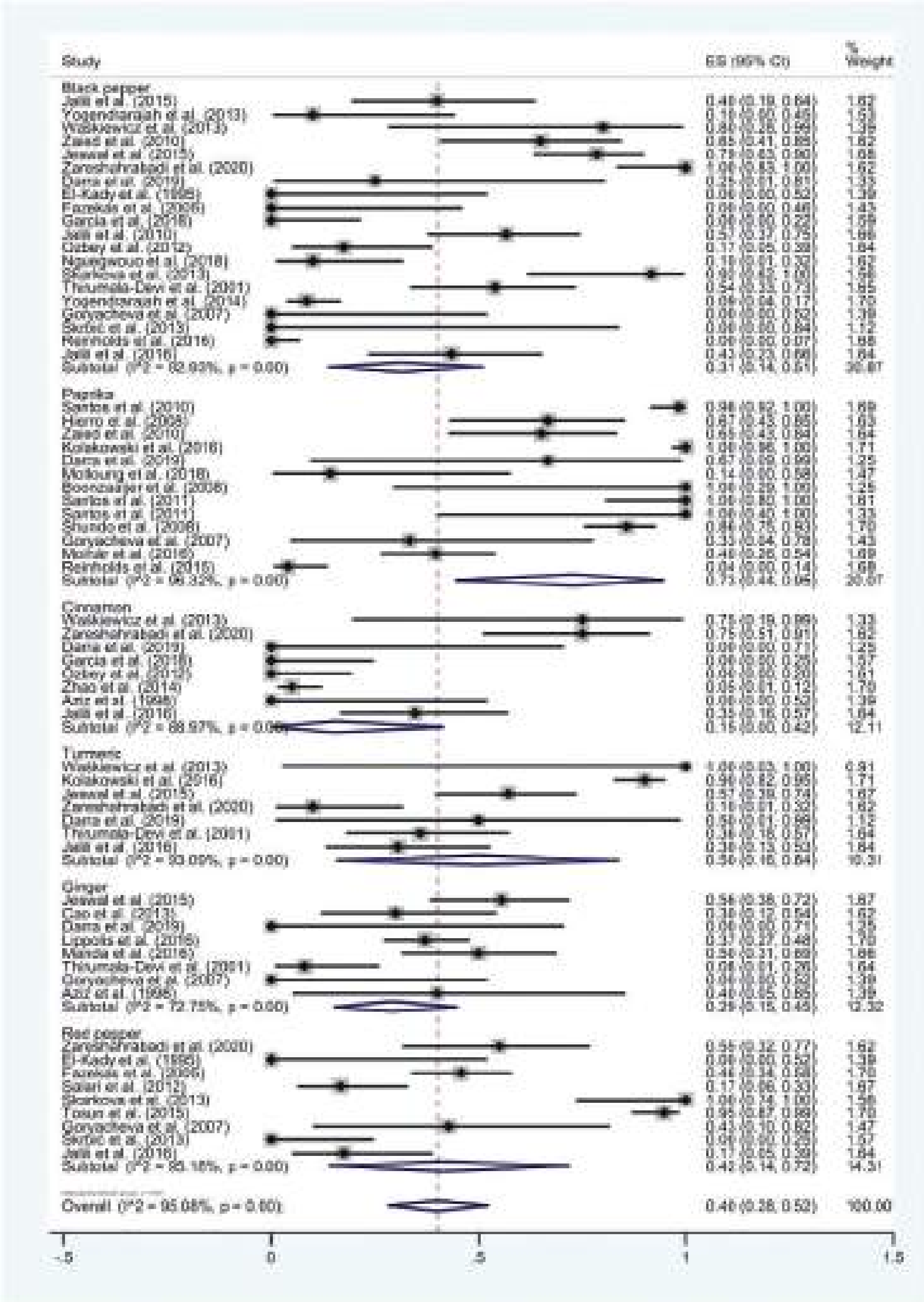

Figure 3. Forest plots for random-effects meta-analysis of prevalence of OTA based on the type of spice. Effect size (ES) is prevalence of mycotoxins in any study.

Table 2. Meta-analysis prevalence of ochratoxin a in spices (%) based on location of study.

Location of study	Number of study	ES*(%)	Lower ES (%)	Upper ES (%)	Relative Weight (%)	P-value	I^2 (%)
Iran	10	0.43	0.23	0.64	16.33	0	89.54
Belgium	2	0.07	0.02	0.14	3.24	0	0
Spain	4	0.96	0.76	1.00	6.26	0	80.93
Poland	3	0.84	0.46	1.00	3.63	0	0
Tunisia	2	0.65	0.50	0.79	3.26	0	0
Canada	2	0.97	0.94	0.99	3.41	0	0
India	6	0.48	0.28	0.68	9.94	0	87.69
China	2	0.08	0.03	0.15	3.32	0	0
Italy	5	0.21	0.00	0.53	6.20	0.31	16.11
Egypt	4	0.05	0.00	0.26	5.56	0.27	24.33
Hungary	3	0.33	0.16	0.53	4.82	0	0
Brazil	3	0.20	0.00	0.94	4.86	0	0
Malaysia	1	0.57	0.37	0.75	1.66	0	0
Nigeria	1	0.37	0.27	0.48	1.70	0	0
Côte d'Ivoire	1	0.50	0.31	0.69	1.66	0	0
South Africa	1	0.14	0.00	0.58	.47	0	0
Turkey	3	0.35	0.00	0.99	4.94	0	0
Netherland	1	1.00	0.29	1.00	1.25	0	0
Cameroon	1	0.10	0.01	0.32	1.62	0	0
Czech Republic	2	0.97	0.85	1.00	3.12	0	0
Russia	4	0.15	0.00	0.44	5.68	0.13	46.57
Latvia	2	0.01	0.00	0.05	3.37	0	0
Serbia	2	0.00	0.00	0.08	2.70	0	0

*Effect size: Prevalence of OTA in any study.

Table 3. Meta-analysis of the prevalence of ochratoxin a in spices by continent.

Continent	Number of study	ES*(%)	Lower ES (%)	Upper ES (%)	Relative Weight (%)	P-value	I^2 (%)
Asia	22	0.41	0.26	0.57	36.19	0	94.06
Europe	30	0.37	0.18	0.59	43.04	0	93.81
Africa	8	0.36	0.21	0.53	12.49	0	75.15
America	5	0.58	0.19	0.92	8.28	0	97.71

*Effect size: Prevalence of OTA in any study.

Table 4. Mean concentration of ochratoxin a in different spices (ng/g).

Type of spice	Number of study	Mean concentration
Black pepper	19	30.57
Cinnamon	8	3.4
Turmeric	6	24.29
Paprika	8	50.66
Ginger	5	17.13
Red pepper	6	4.94

Table 5. Mean concentration of ochratoxin a in different spices (ng/g) based on continent.

Type of spice	Number of study	Mean concentration
Asia	14	32.68
Europe	5	13.22
Africa	2	1.71

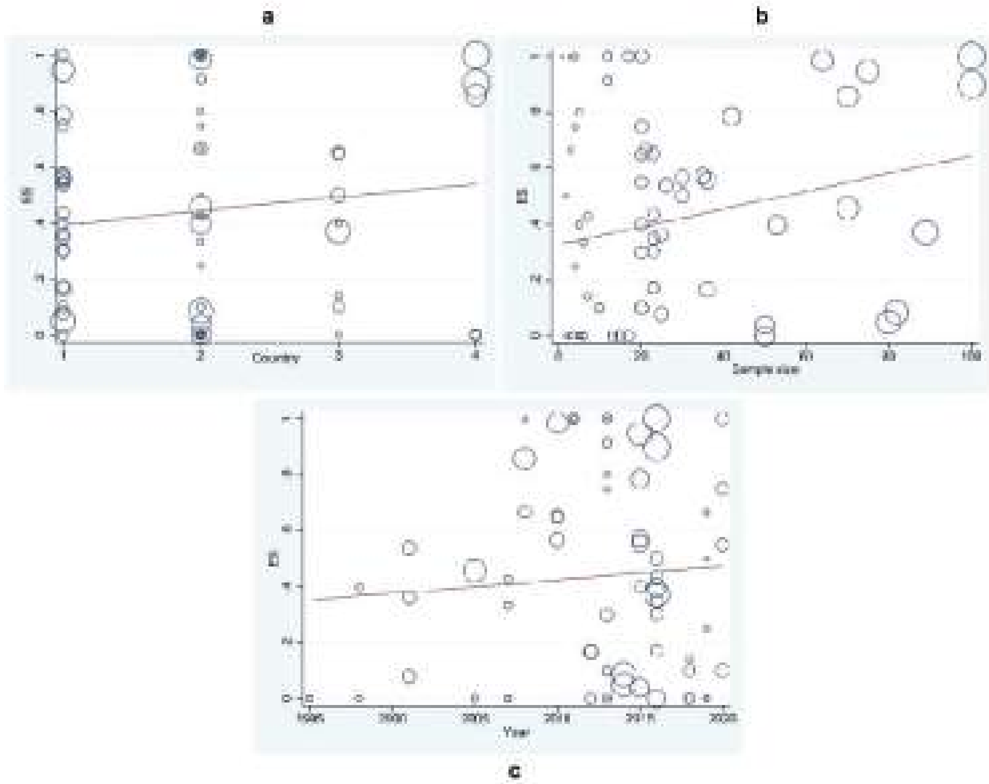

Figure 4. Meta-regression regarding the effect of country (a), sample size (b) and year (c) on prevalence ochratoxin a (OTA) in spices.

10. Meta-regression of data

Meta-regression showed that the association between the prevalence of OTA with sample size (p-value = 0.052), year of study (p-value = 0.56), and continent (p-value = 0.29) were not significant) p-value > 0.05) (Figure 4). According to the publication bias test, publication bias among studies was not significant (P-value = 0.084).

11. Discussion

OTA content is one of the most important factors for evaluating the quality of spices. These products such as paprika, black pepper, turmeric, ginger, red pepper, and cinnamon have been used in daily diets for many years. Unfortunately, despite their benefits, may pose risks due to OTA contamination. The contamination by OTA in the food chain is a serious worldwide issue that can lead to a wide range of health problems [62]. Therefore, due to its toxicity and carcinogenic-related effects, a large number of studies have reported the concentration of this compound in agricultural food crops. However, to the author's knowledge, this is the first quantitative analysis elucidating the overall prevalence and concentration of OTA in different spices. According to our result, the overall prevalence of OTA in the spices was 50%.

Moreover, The highest prevalence of OTA was in paprika (73%), while the lowest prevalence was related to cinnamon (15%). There are many studies that evaluated the content of OTA in spice samples. In a study conducted by Tančinová D et al. (2014) OTA was present in 27.3% of the spice samples [63]. In Tunisia, 57.1% of the spices were contaminated with OTA, with an average concentration of 3.5 ng/g [64]. In another study, Ahmad-Zaidi et al. (2019) reported that 70% of spice samples were positive for OTA, which was higher than the obtained result from this study [65]. Spices are known as plant products with food flavouring, antioxidant, and anti-microbial properties, as well as are susceptible to fungal spoilage. According to the European Commission Regulation No. 1137/2015, the maximum limit of 15 ng/g has been set for spices [22]. Among the analysed studies, 21% (11 out of 52) of the conducted studies exceeded the European standard contamination level for OTA in spices, the highest and the lowest levels were observed in paprika (50.66 ng/g) and cinnamon
(3.4 ng/g), respectively. However, none of the investigated red pepper samples had concentrations more than the permitted levels by the EC. Fazekas et al. (2005) and Santos et al. (2010) investigated the OTA content of different spices. Their finding showed that 11.4% of red pepper and 37% of paprika samples had OTA concentration higher than the guideline level, respectively [28,38]. On the other hand, samples of spice presented a mean OTA contamination of 6.18 ng/g, in a study carried out in Italy [66]. As seen in these studies, there are some differences between our results and other reports about contamination of OTA in spices. The differences in the prevalence and concentration of this mycotoxin can be associated with some factors including climate conditions, geographic location, inappropriate packaging, and improper harvesting procedure which pose an important effect on the OTA production in the final product [67]. In this context, several studies evaluated the effects of different factors on mycotoxin production in contaminated spices. They noticed that the temperatures ranging from 25 to 30°C and moisture contents of about 16% at a water activity of 0.70 can lead to OTA production in these products [68,69]. Among various parameters, storage temperature and the moisture content of the spice are the most important abiotic factors [70]. Subgroup analysis was performed to check the possible effects of country, continent, and type of spices on the prevalence of OTA. Subgroup analysis revealed that the incidence of OTA in Netherland 100% (95% CI: 29–100%) was higher than other countries. Among the countries that presented studies related to OTA contamination in spices, America had a higher prevalence with 58% (95% CI: 19–92%) and it was more prevalent in paprika samples with 73% (95% CI: 44–95%). Based on the conducted studies, OTA concentration was vary in different countries. For example, in studies performed in Italy, Turkey, and Malaysia, the average level of OTA in black pepper was 2.3, 1.82, and 2.16 ng/g, respectively [36,40,45]. In Canada, the OTA concentration was found to be 149 ng/g in paprika [32]. The differences in the concentration and prevalence of OTA in different countries can be due to several reasons such as climates conditions, geographical origin of spice and storage conditions [71]. Alkadri et al. (2014) demonstrated that weather conditions are a critical parameter in the prevalence of mycotoxins in food products [72]. In addition, several researchers have concluded that global warming as one of the main affected factors has increased the prevalence of mycotoxins [73,74]. According to Bayman and Baker

(2006), strains that produce OTA differ between crops and geographical locations [75]. The observed year of study and regional influences can be correlated to weather conditions, in another word, the dry weather and warm seem to lead to increase OTA producing fungi in spices.

Considering Figure 4, the results of meta-regression revealed a positive association between prevalence of OTA with a year of study, country, and sample size, yet these were not statistically significant ($P > 0.05$). This could be due to several factors including economical parameters, rainfall rate, agriculture, and preventive practices in different regions. Given the frequency of OTA in spices and the stability of this toxin, consumption of such products could be a matter of health concern due to their possible toxic effects.

The main strength of the present study was that this is the first meta-analysis to evaluate the prevalence and concentration of OTA in spices. Prior to this meta-analysis, the evidence base was not uniform and needed a quantitative investigation which we have performed. However, there are some limitations such as the small samples size that need to be addressed in this meta-analysis.

12. Conclusion

In the current study, the prevalence and concentration of OTA in spices were investigated based on defined subgroups such as country, continent, and type of spice products. Meta-regression was also conducted between the prevalence of OTA in spice with a year of study, sample size, and country. The highest prevalence of OTA was observed in the paprika samples, while the lowest values were attributed to cinnamon. On the other hand, the rank of spices regarding the concentration of this toxin was ordered as paprika > black pepper > turmeric > ginger > red pepper > cinnamon. Meta-regression indicated that the year of study, sample size, and country can affect the incidence of OTA in spices. The outcome of this meta-analysis can be used for risk assessment model development, aiming to help the government and industries for finding a specific way to reduce exposure to this mycotoxin through the consumption of spice products.

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No potential conflict of interest was reported by the author(s).

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