Impacts of soil and water fluoride contamination on the safety and productivity of food and feed crops: A systematic review

Original
Impacts of soil and water fluoride contamination on the safety and productivity of food and feed crops: A systematic review / Rizzu, Margherita; Tanda, Alberto; Cappai, Chiara; Roggero, Pier Paolo; Seddaiu, Giovanna. - In: SCIENCE OF THE TOTAL ENVIRONMENT. - ISSN 0048-9697. - 787:(2021), p. 147650. [10.1016/j.scitotenv.2021.147650]

Published
DOI:10.1016/j.scitotenv.2021.147650

Impacts of soil and water fluoride contamination on the safety and productivity of food and feed crops: A systematic review / Rizzu, Margherita; Tanda, Alberto; Cappai, Chiara; Roggero, Pier Paolo; Seddaiu, Giovanna. - In: SCIENCE OF THE TOTAL ENVIRONMENT. - ISSN 0048-9697. - 787:(2021), p. 147650. [10.1016/j.scitotenv.2021.147650]

Science of the Total Environment

Impacts of soil and water fluoride contamination on the safety and productivity of food and feed crops: A systematic review

--Manuscript Draft--

Manuscript Number:	STOTEN-D-21-02700R1
Article Type:	Review Article
Keywords:	pollution; yield reduction; Oxidative stress; Risk Assessment; hazard index; Fluorosis
Corresponding Author:	Margherita Rizzu, Ph.D. University of Sassari: Universita degli Studi di Sassari Sassari, SS ITALY
First Author:	Margherita Rizzu, Ph.D.
Order of Authors:	Margherita Rizzu, Ph.D.
	Alberto Tanda
	Chiara Cappai
	Pier Paolo Roggero
	Giovanna Seddaiu
Abstract:	Although a strong connection between the environmental fluoride contamination and the fluorosis disease is nowadays worldwide well documented, the knowledge on the fluoride contamination levels of cultivated crops at the basis of the human food-chain is limited and fragmented. Adopting a systematic approach, this study reviews the available literature concerning the impacts of soil and water fluoride pollution on the safety and productivity of food and feed crops at a global scale, with the aim to provide a comprehensive overview of the current state of the art. The analyses of literature highlighted that food and feed crops exposed to soil and water fluoride pollution may reach concentrations of fluoride potentially harmful to human health. Nevertheless, despite the efforts already made to assess the crop fluoride accumulation in contaminated areas of India and China, the present study brings to light the lack of knowledge still existing on this issue for some regions strongly affected by environmental fluoride contamination such as the East African Rift Valley. Concerning the impacts of fluoride on cultivated crops, many authors observed that fluoride can produce toxic effects on plants leading to oxidative stress, reduction in chlorophyll content, alterations in the levels of proline, betaine, soluble sugars, nitrogen and macro and micronutrients. However, the appearance of symptoms such as visible injuries, reduced root and shoot length and yield decline was not always observed, also at high levels of fluoride exposure, and in some cases, the biomass production was even stimulated by increasing fluoride doses.
Response to Reviewers:	We are very grateful to the referees for the analysis of the manuscript and the very valuable suggestions. In the "Response to Reviewers comments" file we have reported our comments and responses to the reviewer’s suggestions. As concern the Supplementary Material, as indicated in the guidelines, we did not annotate any corrections and switched off the 'Track Changes' option in Microsoft Word in the updated files that we uploaded. However, since we have also made some revisions to the supplemental files, to allow reviewers to track the corrections made, we have included the tracked versions of the supplemental files in the "Supplemental files with Changes Marked" file.

Impacts of soil and water fluoride contamination on the safety and productivity of food and feed crops: A systematic review

Margherita Rizzu [a,b,*], Alberto Tanda[a,b], Chiara Cappai[a,b], Pier Paolo Roggero[a,b], Giovanna Seddaiu[a,b]

[a] Dipartimento di Agraria, University of Sassari, Viale Italia 39, 07100, Sassari, Italy

[b] Desertification Research Centre, NRD, University of Sassari, Viale Italia 39, 07100, Sassari, Italy

mrizzu@uniss.it, tandaalberto@gmail.com, ccappai@uniss.it, pproggero@uniss.it, gseddaiu@uniss.it.

*Corresponding author: Margherita Rizzu

Tel.: +39 3454034148

E-mail: mrizzu@uniss.it

Address: Viale Italia 39, 07100, Sassari, Italy;

CRediT author statement:

Margherita Rizzu: Conceptualization, Methodology, Investigation, Data Curation, Writing - Original Draft preparation, Visualization. Alberto Tanda: Investigation, Data Curation, Writing- Original draft preparation. Chiara Cappai: Investigation, Draft preparation. Pier Paolo Roggero: Writing - Reviewing and Editing, Supervision. Giovanna Seddaiu: Conceptualization, Writing - Reviewing and Editing, Supervision, Resources and project management.

Reviewer #2

Comments to Author	Responses
1. The Graphical Abstract does not give much useful information. It should be reconsidered.	Thank you for this recommendation, we have redrawn the graphical abstract using a more informative type of graph
2. The first two highlights are meaningless. They told only what the authors did, but did not tell the significant findings that the authors obtained.	As suggested, we rewrote the highlights focusing on the significant findings that were obtained in the Systematic Review
3. There should be only one paragraph in the abstract.	We deleted the carriage return to make the abstract a single paragraph.
4. The first sentence should cite two or three more latest references, as you said the problem is well recognized. It is unconvincing to cite only one reference. In addition, the currently cited reference is very old (published more than 20 years ago). So please cite some references that were published in the last 5 years. Maybe the following ones can be considered. Li, P., He, X., Li, Y., Xiang, G. 2019. Occurrence and health implication of fluoride in groundwater of loess aquifer in the Chinese Loess Plateau: a case study of Tongchuan, northwest China. Exposure and Health 11(2):95-107. https://doi.org/10.1007/s12403-018-0278-x He, X., Li, P., Ji, Y., Wang, Y., Su, Z., Elumalai, V. 2020. Groundwater arsenic and fluoride and associated arsenicosis and fluorosis in China: occurrence, distribution and management. Exposure and Health 12(3):355-368. https://doi.org/10.1007/s12403-020-00347-8 Wu, J., Li, P., Qian, H. 2015. Hydrochemical characterization of drinking groundwater with special reference to fluoride in an arid area of China and the control of aquifer leakage on its concentrations. Environmental Earth Sciences 73(12):8575-8588. https://doi.org/10.1007/s12665-015-4018-2 Subba Rao, N., Ravindra, B., Wu, J. 2020. Geochemical and health risk evaluation of fluoride rich groundwater in Sattenapalle Region, Guntur district, Andhra Pradesh, India. Human and Ecological Risk Assessment 26(9):2316-2348. https://doi.org/10.1080/10807039.2020.1741338 Wu, J., Sun, Z. 2016. Evaluation of shallow groundwater contamination and associated human health risk in an alluvial plain impacted by agricultural and industrial activities, mid-west China. Exposure and Health 8(3):311-329. https://doi.org/10.1007/s12403-015-0170-x	As suggested, we added the following three more latest references to the first sentence: He, X., Li, P., Ji, Y., Wang, Y., Su, Z., Elumalai, V. 2020. Groundwater arsenic and fluoride and associated arsenicosis and fluorosis in China: occurrence, distribution and management. Exposure and Health 12(3):355-368. https://doi.org/10.1007/s12403-020-00347-8 Subba Rao, N., Ravindra, B., Wu, J. 2020. Geochemical and health risk evaluation of fluoride rich groundwater in Sattenapalle Region, Guntur district, Andhra Pradesh, India. Human and Ecological Risk Assessment 26(9):2316-2348. https://doi.org/10.1080/10807039.2020.1741338 Wu, J., Sun, Z. 2016. Evaluation of shallow groundwater contamination and associated human health risk in an alluvial plain impacted by agricultural and industrial activities, mid-west China. Exposure and Health 8(3):311-329. https://doi.org/10.1007/s12403-015-0170-x

5. Line 61, such for example should be such as	We have corrected the sentence as suggested (Line 61)
6. Line 66, agricultural-related as should be agricultural-related activities such as	We have corrected the sentence as suggested (Line 66)
7. Lines 170 and 172, Zhonglei is not the family name of the Chinese author, and it is the given name of the Chinese scholar. So please recheck the names of the authors from the references.	As recommended, we have rectified the sentences using the correct family name of the author (Text: Line 178 and 181; References: 971, 997 Supplemental File 3: Table 5: reference #3). We double-checked all the references and corrected the following typing or formatting mistakes: **Line 325 and 415.** Szostek and ~~Ciecko~~ Ciećko **Line 659.** ~~Interantional~~ International **Line 696.** Asian Journal of Experimental Sciences **Line 716.** ~~2016~~2016a. **Line 719**. ~~2016~~2016b. **Line 791.** doi:~~https://doi.org/~~10.1007/s10653-020-00568-5. **Line 802.** South Asian Journal of Experimental Biology **Line 868.** doi:~~https://doi.org/~~10.1371/journal.pmed.1000097. **Line 884.** ~~Physiol. Mol. Biol.~~Physiology and Molecular Biology of Plants **Supplemental File 3: Table 5: reference #13:** ~~YePu, et al.~~ Li, et al. (2018) The same typing and formatting mistakes were corrected also in **Supplemental File 2 - List of publication included in the Systematic Review**
8. Lines 454-455, this sentence needs a reference.	Please note that as per a suggestion of reviewer # 3 we have rephrased the sentence in question as follows: At a global level, it is estimated that around 200 million people are at risk of hazardous exposure to fluoride, including about 66 million people in India and 45 million in China with a high prevalence also found in South America and Africa (Edmunds and Smedley, 2013). The bibliographic reference to which the information reported in the entire sentence refers is: Edmunds and Smedley, 2013.
9. DOI information is suggested to add after each of the references. This will help readers to track the literature.	As suggested, we added the DOI information after each reference for which this information was possible to find.

10. There are so many tables. Some tables that are not so important can be put into supplementary or can be explained using plain text. Big tables will take up too many pages. I think inclusion of 4-5 tables may be enough for the review article.	As per your advice, we have left in the text only the first 4 tables (relating to materials and methods) and we have putted the over-size tables in the supplemental materials (Supplemental File 3 - Over-size tables).

Reviewer #3

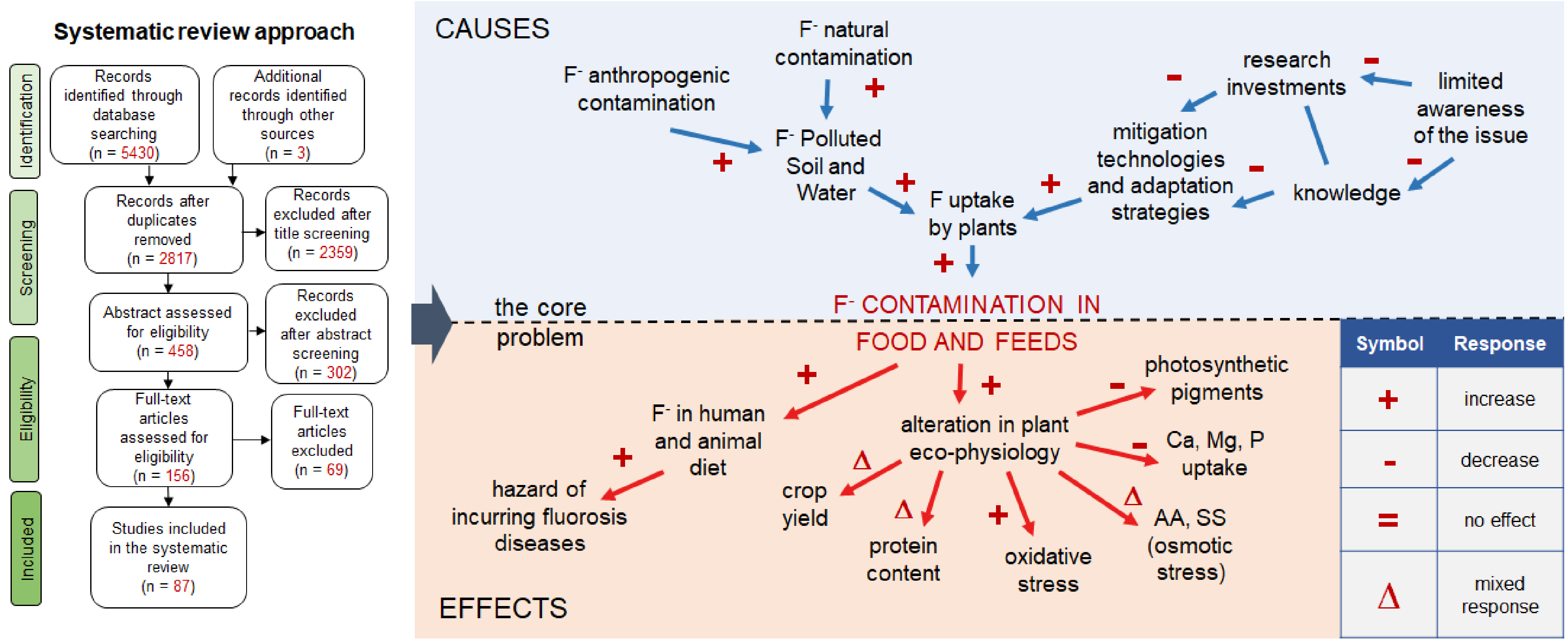
Referee's comments	**Responses**
1. The Graphical Abstract of the paper is not informative and meaningful, and should be redrawn.	Thank you for this recommendation, we have redrawn the graphical abstract using a more informative type of graph
2. The highlights didn't accurately reflect the main points of the paper, they should be rewritten.	As recommended, we rewrote the highlights focusing on the main findings that were obtained in the Systematic Review
3. Line 366, ad at the end of the line should be as.	We have corrected the typo as indicated (Line 398)
4. Line 455, what do you mean by"66 of which in India and 45 in China"?	We have rephrased the sentence indicated to make it more understandable as follows (line 486): At a global level, it is estimated that around 200 million people are at risk of hazardous exposure to fluoride, including about 66 million people in India and 45 million in China with a high prevalence also found in South America and Africa (Edmunds and Smedley, 2013).
5. For the 3.4.5. Effects on nutrients balance, it's really not nutrients balance.	As suggested, we have modified the paragraph title as follow (line 413): *3.4.5. Effects on nutrients ~~balance~~ uptake*
6. The title of 3.4.7 is Effects on protein, nitrogen forms, ash, fat and fibre contents, but for the nitrogen, the content of the discussion is not "nitrogen forms".	As suggested, we have modified the paragraph title as follow (line 452): *3.4.7. Effects on protein, nitrogen ~~forms~~, ash, fat and fibre contents* We have also corrected this information in Table 3 and Table 3a (SF1) (last row) and in the title of SF3 - Table 13 - Effects of increasing doses of soil or water fluoride on the content of protein, nitrogen ~~forms~~ (N-tot: total nitrogen, N-prot: protein nitrogen, N-nitrate: nitrate nitrogen), ash, fat and fibre in different vegetable species. (Please note that Table 13 has been moved to Supplemental File 3 (SF3) as per the suggestion of reviewer # 2).

Reviewer #4

Referee's comments	**Responses**
1. the level of F- in the groundwater in a particular region if correlated with the presence of F- bearing minerals and the depth of the water table, can be another layer of information which can greatly enhance the utility of the review. 3. A correlation between the occurrence of high F- in soil and groundwater and the occurrence of F-induced diseases (fluorosis) among the inhabitant of the area, would add weight to the review.	Thank you for these interesting suggestions, we checked whether the further information you recommended (presence of F- bearing minerals, depth of the water table, and correlation between the occurrence of high F- in soil and groundwater and occurrence of F- induced diseases among the inhabitant of the area) was reported in the field studies included in the present systematic review (SR) in order to add new useful information layers to those reported in table 5 (now in Supplemental File 3 as per suggestion of reviewer #2). Unfortunately, most of the studies included in the present SR, following the *research method* and the *keywords* and the *inclusion and exclusion criteria* defined in the Review Protocol (Table 1), did not report the suggested further information. Expanding the research to further studies would lead beyond the boundaries of the present SR, which has as its core topic the impacts of soil and water fluoride pollution on the safety and the productivity of food and feed crops at a global scale.
2. The conclusion is very general and speculative. The conclusion should be synthesis of the findings from the study or review.	Thank you for this precious comment. As recommended, we reviewed the conclusions of the work, agreeing on the need to give it a focus more oriented to report the synthesis of the findings of the systematic review work and clear indications both for future research perspectives and in terms of agronomic management of crop systems contaminated by fluoride. During the review of the conclusions we found that in order to summarize the clearest messages possible both as regards the impact of fluoride on crop yields, and as regards the attitude of the crops with respect to the bio-accumulation of fluoride, some small integrations were necessary also in the results paragraph. In paragraph 3.4.1. (Effects on growth and biomass) we inserted a brief integration with respect to aspects related to crop yields (line 330). In paragraph 3.3.1., concerning the crop accumulation pattern, we inserted an integration regarding the transfer factor (line 229). We have in fact included the calculation of this index, based on the data already reported, in table 6, which allowed us to better assess the accumulation trend in plant tissues of crops subjected at the increasing doses of contamination. The TF calculation method was reported in M&M (line 134). In paragraph 4 (Knowledge gaps and future research perspectives)

	we then discussed the limits of the proposed index, which it was possible to calculate based on the available data, with reference to another index, the bio-concentration factor highlighting the need to use the latter to obtain a comparison between crops based only on the crops bio-accumulation capacity and not biased by other interacting soil factor.

Graphical Abstract



Highlights

1. ~~Information on the impacts of F pollution on crop yield and safety is limited and fragmented.~~
2. ~~We gather all the available literature data on this topic through a systematic approach.~~

1. Plants tend to accumulate fluoride mostly in the root system
2. Accumulation of F in plant tissues is dose-dependent with some exceptions
3. F contamination of food crops can represents an actual health hazard in polluted areas
4. F can alter chlorophyll levels, plant physiology and can induce oxidative stress

~~4.~~5. Evidences of F affecting crop yields are often contradictory even at high F levels

Impacts of soil and water fluoride contamination on the safety and productivity of food and feed crops: A systematic review

Margherita Rizzu [a,b,*], Alberto Tanda[a,b], Chiara Cappai[a,b], Pier Paolo Roggero[a,b], Giovanna Seddaiu[a,b]
[a] Dipartimento di Agraria, University of Sassari, Viale Italia 39, 07100, Sassari, Italy
[b] Desertification Research Centre, NRD, University of Sassari, Viale Italia 39, 07100, Sassari, Italy
mrizzu@uniss.it, tandaalberto@gmail.com, ccappai@uniss.it, pproggero@uniss.it, gseddaiu@uniss.it.

*Corresponding author: Margherita Rizzu
Tel.: +39 3454034148
E-mail: mrizzu@uniss.it
Address: Viale Italia 39, 07100, Sassari, Italy;

CRediT author statement:

Margherita Rizzu: Conceptualization, Methodology, Investigation, Data Curation, Writing - Original Draft preparation, Visualization. Alberto Tanda: Investigation, Data Curation, Writing- Original draft preparation. Chiara Cappai: Investigation, Draft preparation. Pier Paolo Roggero: Writing - Reviewing and Editing, Supervision. Giovanna Seddaiu: Conceptualization, Writing - Reviewing and Editing, Supervision, Resources and project management.

Abstract

Although a strong connection between the environmental fluoride contamination and the fluorosis disease is nowadays worldwide well documented, the knowledge on the fluoride contamination levels of cultivated crops at the basis of the human food-chain is limited and fragmented. Adopting a systematic approach, this study reviews the available literature concerning the impacts of soil and water fluoride pollution on the safety and productivity of food and feed crops at a global scale, with the aim to provide a comprehensive overview of the current state of the art. The analyses of literature highlighted that food and feed crops exposed to soil and water fluoride pollution may reach concentrations of fluoride potentially harmful to human health. Nevertheless, despite the efforts already made to assess the crop fluoride accumulation in contaminated areas of India and China, the present study brings to light the lack of knowledge still existing on this issue for some regions strongly affected by environmental fluoride contamination such as the East African Rift Valley. Concerning the impacts of fluoride on cultivated crops, many authors observed that fluoride can produce toxic effects on plants leading to oxidative stress, reduction in chlorophyll content, alterations in the levels of proline, betaine, soluble sugars, nitrogen and macro and micronutrients. However, the appearance of symptoms such as visible injuries, reduced root and shoot length and yield decline was not always observed, also at high levels of fluoride exposure, and in some cases, the biomass production was even stimulated by increasing fluoride doses.

Keywords: pollution, yield reduction, oxidative stress, risk assessment, hazard index, fluorosis.

1. Introduction

The association between excessive environmental fluoride occurrence and the high rate of fluorosis in the populations of polluted areas is nowadays well recognized (He, et al., 2020, Ozsvath, 2009, Subba Rao, et al., 2020, Wu and Sun, 2016). The prolonged exposure to high fluoride doses can lead, in fact, to a series of major illnesses that involve the dental apparatus and skeletal system but also, as recently examined, non-skeletal tissues as internal organs, nervous, reproductive and immune systems (Wei, et al., 2019). Although low-fluoride intakes have been recognised to have positive effects on the prevention of dental caries, moderate chronic ingestion, particularly during childhood, is known to provoke the appearance of black spots on teeth and in most severe cases their loss. Skeletal system disorders appear with the protracted intake of high fluoride doses with symptoms that comprise bone deformities, ligaments calcification and associated back, knee, shoulder and neck pain with difficulties in movements and in proper walking (Bharati, et al., 2005, WHO, 1999, 2011).

Endemic fluorosis is prevalent in at least 25 countries with the highest incidence in India, China and various African regions (Vithanage and Bhattacharya, 2015), but groundwater with concentrations above the WHO guideline limit for drinking-water (1.5 mg L^{-1}) have been found in many parts of the world. Beyond China and India, affected regions are Sri Lanka, North and West African countries (Tunisia, Libya, Sudan, Senegal, Ghana, Ivory Coast), the East African Rift Valley (Kenya, Tanzania, Ethiopia, Uganda and Rwanda), South Africa, central Argentina, northern Mexico and Pakistan (Edmunds and Smedley, 2013).

The sources of fluoride contamination can be both natural and anthropogenic with the firsts being paramount (Amini, et al., 2008). Natural sources are related to geogenic processes that are primarily responsible for groundwater pollution, such ~~for example~~as the weathering of F-rich minerals and the release of fluoride due to volcanic activities, fumarolic gases, hydro-geothermal vents and marine aerosols. Contamination from anthropogenic activities can be significant on a local scale and may be either of industrial origin, such as the release of wastes from aluminium smelters, effluents from coal-based power stations and factories processing various materials (e.g glass, ceramic, plastics, pesticides, disinfectants, etc.), or agricultural-related such as the long-term uncontrolled use of phosphatic fertilizer or the irrigation with fluoride-enriched water (Ali, et al., 2016, Kimambo, et al., 2019, Singh, et al., 2018)

Through the polluted soil, water, and air, fluoride can enter the food-chain (Vithanage and Bhattacharya, 2015). After drinking water, in fact, the consumption of contaminated food products is considered another important source of fluoride exposure for human organisms (Brahman, et al., 2014, WHO, 2011). Furthermore, the contamination of the plant growth environment can lead to the manifestation of toxic effects in food crops with consequent yield and nutritional quality reduction and related economic losses (Ahmed, et al., 2019a, Bustingorri and Lavado, 2014).

Several field-scale explorative trials and controlled experiments have been conducted in various contaminated regions of the world to investigate the accumulation of fluoride in crops and the effects on their productivity, nevertheless, the information is still fragmented. Even though, in fact, numerous studies have considered and examined the worldwide environmental fluoride occurrence, particularly in groundwater systems (Amini, et al., 2008, Edmunds and Smedley, 2013, Kimambo, et al., 2019, Vithanage and Bhattacharya, 2015), and various overviews have been conducted on fluoride toxicity in plants (Baunthiyal and Ranghar, 2014, Baunthiyal and Ranghar, 2015, Choudhary, et al., 2019, Singh, et al., 2018, Yadu, et al., 2016), no systematic reviews have been performed concerning the impacts of soil and water fluoride pollution on the safety and the productivity of food and feed crops at a global scale.

With the aim to provide a comprehensive overview on this topic and bring to light the gaps of knowledge, this work attempted to gather all the existing scientific literature on the impacts of the environmental fluoride pollution on crop productivity and safety.

The findings of this review are intended to suggest future research directions to scientists toward a better understanding of the relationships between fluoride contamination and food safety and production as well as informing the development of possible mitigation and adaptation strategies in the affected areas.

2. Review methods

The systematic literature review followed the methodological approach reported by existing guidelines (Bilotta, et al., 2014, Collaboration for Environmental Evidence, 2013, Pullin and Knight, 2009, Pullin and Stewart, 2006). A review protocol was implemented defining the connotations of the systematic literature search, the inclusion/exclusion criteria and the data extraction forms (Supplemental File 1 - SF1).

2.1. Resources

Academic search engines such as ISI Web of Science (Web of Science Core Collection plus other databases such as Bioabs, Kjd, Medline, Rsci, Scielo), PubMed, Scopus, Science Direct, JSTOR, Agricola, Fluorideresearch.org and Cab Abstracts were used. Advanced search options were considered entering the following keywords: *fluoride OR fluorine*, in the title field, *AND crop OR plant OR vegetation OR grasses OR vegetables OR agriculture*, in the other fields. The search was restricted to the English language, and the timespan went from 1985 to 2020. To refine the results, the search conducted on the Web of Science Core Collection and the Scopus database was limited to the following subject areas:

- for the Web of Science Core Collection: *Environmental sciences, Toxicology, Water resources, Plant sciences, Soil science, Agronomy, Ecology, Agriculture multidisciplinary, Multidisciplinary sciences, Biology, Forestry, Horticulture Agricultural engineering, Physiology, Agriculture dairy animal science, Environmental studies*
- for the Scopus database: *Environmental Science, Agricultural and Biological Sciences, Multidisciplinary, Decision Sciences*

2.2. Review process

Records were stored in a reference manager software database and duplicates were eliminated. The article screening was performed following a stepwise process according to the established inclusion criteria (Table 1). A first selection was conducted on the basis of the publication title, in the second stage abstracts were assessed and finally, the remaining articles were filtered revising the whole paper. In case of doubts about the pertinence of a record, this was included and further evaluated in the next stage. A subset of the references was revised by two further independent reviewers in order to assess the reliability of the application of the inclusion criteria. The final numbers of articles recovered, duplicated, accepted and excluded were annotated to produce an accurate PRISMA flow diagram (Preferred Reporting Items for Systematic reviews and Meta-Analyses) (Moher, et al., 2009). The list of the papers that were finally included is reported in the Supplemental File 2~~.~~ (SF2).

2.3. Data extraction and analysis

From the final subset of articles, available qualitative (Table 2) and quantitative (Table 3) information was extracted. If the data were not reported in the text, they were extracted from tables and graphs.

For each extracted variable, the percentages increase/decrease (Δ%) from control values to those of treated subjects were calculated and data were summarized in Tables ~~8-13.~~5-13 included in Supplemental File 3 (SF3).

In Table 6 (SF3), the Transfer Factor (TF) in the edible parts was calculated by the ratio between the concentration of fluoride of the edible organs and the concentration of total fluoride in the soil (Ding, et al., 2018)~~.~~. Furthermore, the accumulation pattern was reported. The TF index allows to assess the accumulation trend in plant tissues of crops subjected at increasing doses of contaminant. When TF >1, the concentration of fluoride in the plant tissues is higher than the concentration of total fluoride in soil, indicating a hyper-accumulator behaviour in the considered plant organ.

3. Results

3.1. Characteristics of the studies included in the systematic review

A total of 87 studies was retrieved through the process of the systematic review (Figure 1), with 77 % of the collected articles published after or in the year 2010.

Field-scale studies, pot experiments, hydroponic experiments and multi-experiments studies were found. Some of them reported exclusively data on fluoride accumulation in crops, from others it was possible to get only data on the effects of fluoride on plants and further articles included both types of data (Table 4).

Around 46 % of the studies were focused on soil pollution, 37 % on water pollution and the remaining 17 % on both sources of fluoride contamination.

Among the studies conducted under controlled conditions (pot and hydroponic experiments), in the 74% of the cases, NaF was used as a pollutant to contaminate the source of exposure (soil or water), KF was used in the 11% of the studies, NH_4F in another 11% while AlF and HF in the 4%.

3.2. Fluoride in the water-soil-plant system of different areas of the world and human health hazard

The areas in which the greatest number of studies has been conducted were India (~42%, 16 studies) and China (~32%, 12 studies), where the considered environmental fluoride contamination was mostly of natural origin. Concerning the other regions, just two field-scale studies (~5%) were found for Pakistan and one field-scale study (~3%) for each of the following regions was found: Argentina, Ethiopia, Iran, Nigeria, New Zealand, Poland, Russia and Tanzania (Figure 2).

Concerning India, the majority of the studies regarded the areas of Rajasthan and West Bengal, furthermore, other experiments were conducted also in Andhra Pradesh, Telangana, Bangalore, Uttar Pradesh and Bihar (SF3 - Table 5). In general, the different studies considered a wide variety of food crops, including grain crops, pulses, horticultural crops, leafy vegetables and tubers. The lowest value of soil total fluoride concentration (6.7 mg $F^- kg^{-1}$) was found by Nagaraju et al. (2017) in Talupula, Anantapur District, Andhra Pradesh while the highest (681.0 mg $F^- kg^{-1}$) was detected in Rajasthan by Saini et al. (2013). The soil water-soluble fluoride varied from 0.3 mg $F^- kg^{-1}$ (Lakshmi, et al., 2016) in Aatmakoor Mandal, Nalgonda district, Telangana, to 73.9 mg $F^- kg^{-1}$ in Rajasthan (Saini, et al., 2013). Concerning groundwater, the fluoride concentration ranged from 0.3 mg $F^- L^{-1}$ in Birbhum district to 21.5 mg $F^- L^{-1}$ in Bangalore (Begum, et al., 2008, Mondal and Gupta, 2015). The lowest contents of fluoride in various vegetable species (< 4.2 mg $F^- kg^{-1}$ DM) were observed in the regions of Nowapara and Junidpur, Birbhum district and in Nalgonda district, Telangana (Lakshmi, et al., 2016, 2017a, 2017b, Pal, et al., 2012), while the greatest value was recorded in *Brassica oleracea* L. (296 mg $F^- kg^{-1}$ DM) by Begum et al. (2008) in Bangalore.

Regarding China, six out of twelve field-scale studies concerned the uptake and accumulation of fluoride in tea plant (*Camellia sinensis* (L.) O. Kuntze) which is well known to be one among the fluoride hyper-accumulator species (Cronin, et al., 2000). The concentration of fluoride in young tea leaves varied from a minimum of 49.0 mg $F^- kg^{-1}$ DM found by ~~Zhonglei et al.~~ Xie, et al. (2007), up to 808.0 mg $F^- kg^{-1}$ DM observed by Fung et al. (1999) in Guangdong province. Mature leaves were found to have higher concentrations compared to young ones, ranging from 221.0 mg $F^- kg^{-1}$ DM ~~(Zhonglei, et al., 2007)~~ (Xie, et al., 2007) to 2919.0 mg $F^- kg^{-1}$ DM in Lantau Peak of Lantau Island (Fung, et al., 2003). The fluoride accumulation in edible parts of various food crops observed by different authors in China ranged from a value of 0.1 mg $F^- kg^{-1}$ DM in cabbage up to 34.7 mg $F^- kg^{-1}$ DM in pumpkins leaves (He, et al., 2020), and the concentration of fluoride in wheat grains (0.6-7.2 mg $F^- kg^{-1}$ DM) was found, in most of the cases, to be higher than the national edible health standard of China (CMH, 2012) ($\leq$ 1.5 mg kg^{-1}) (Li, et al., 2019a, Li, et al., 2017, Wang, et al., 2012, Yu, et al., 2018, Zheng and Sun, 2011). Higher concentrations were found in roots, leaves and straw of wheat grown in the region of Baiyin, Gansu province and Yangtze River outfall region and in roots and leaves of maize, with the greatest value (542 mg $F^- kg^{-1}$ DM) observed in Gansu province in roots

(Li, et al., 2019a, Li, et al., 2017, Wang, et al., 2012). In this area also the highest concentration of fluoride were recorded both in soil (total fluoride: 4987 mg F^{-} kg^{-1}; water-soluble fluoride: 59 mg F^{-} kg^{-1}) and water (82 mg F^{-} L^{-1}) (Li, et al., 2017). The lowest values of soil total fluoride (82 mg F^{-} kg^{-1}) and water fluoride (0.2 mg F^{-} L^{-1}) were observed in Shihezi, Xinjiang by Yu et al. (2018) while the minimum soil water-soluble fluoride (0.04 mg F^{-} kg^{-1}) was found by Ruan and Wong (2001) in Jintan County (Jiangsu Province).

Environmental fluoride pollution of natural origin was also found in the water-soil-plant systems of Argentina, Ethiopia, Nigeria, Pakistan and Tanzania (Brahman, et al., 2014, Dagnaw, et al., 2017, De Troiani, et al., 1987, Kazi, et al., 2019, Okibe, et al., 2010, Rizzu, et al., 2020), while anthropogenic sources of fluoride contamination were identified in Poland, New Zealand and Russia. In Poland, the old Warta reservoir near the town of Luboń was severely contaminated by the wastes from a nearby chemical plant (Jezierska-Madziar and Pinskwar, 2003), in New Zealand Loganathan et al. (2001) studied the effects of the long-term application of P-fertilizer on the top-soil fluoride concentration (SF3 - Table 5) while in Russia Sokolova et al. (2019) studied the effects of fluoride contaminated soils 0.5 km from the IrkAZ (one of the largest enterprises in aluminium industry in Russia) on the productivity and fluoride uptake of some field crops.

Some of the abovementioned authors, as well as assessing the fluoride accumulation in food crops also conducted nutritional surveys among the populations of the contaminated areas in order to estimate a hypothetical fluoride daily ingestion (estimated daily intake, EDI) associated with the consumption of the studied crops and the related hazard index (HI) which represents how many times the effective intake exceeds the recommended dose. In many cases, the cumulative EDI from the diet and drinking water exceeded the recommended value (HI > 1) with children and teenagers being the categories considered at major risk (Bhattacharya, et al., 2017, Brahman, et al., 2014, He, et al., 2020, Jha, et al., 2008a, Kazi, et al., 2019, Rizzu, et al., 2020).

3.3. Fluoride uptake and partitioning under controlled conditions

Among the analysed publications concerning pot and hydroponic experiments, it was possible to get data on fluoride accumulation in plant tissues of 31 different species including cereals (*Hordeum vulgare* L., *Oryza sativa* L., *x Triticosecale* Wittm., *Triticum aestivum* L., *Zea mays* L.), pseudo-cereals (*Amaranthus gangeticus* L., *Amaranthus viridis* L.), pulses (*Glycine max* L. Merrill, *Lupinus angustifolius* L., *Lupinus luteus* L., *Medicago sativa* L., *Onobrychis viciifolia* Scop., *Pisum sativum* L.), horticultural species (*Abelmoschus esculentus* (L.) Moench, *Allium cepa* L., *Coriandrum sativum* L., *Ipomoea aquatica* Forssk., *Lactuca sativa* L., *Spinacea oleracea* L.), in particular species belonging to the Brassicaceae (*Brassica chinensis* L., *Brassica juncea* L., *Brassica napus* L., *Brassica oleracea* L., *Raphanus sativus* L.) and Solanaceae families (*Lycopersicon esculentum* L., *Solanum tuberosum* L.) and further cultivated species (*Camellia japonica* L., *Camellia sinensis* (L.) O. Kuntze, *Olea europaea* L., *Phacelia spp*. Juss., *Saccharum officinarum* L.) (SF3 - Table 6).

3.3.1. Fluoride Transfer Factor (TF) in edible parts and accumulation pattern

An overall decreasing trend in the TF (which remains always < 0.4) calculated for edible parts of lady's finger, onion, radish and soybean was observed in several studies where plants were treated with increasing doses of NaF in soil (20-1000 mg F^- kg^{-1}). A decreasing behaviour was observed also in the case of spinach (50-800 mg F^- kg^{-1}) with TF of leaves reaching higher values (1-0.5) at the lowest concentrations (< 200 mg F^- kg^{-1}). Potato tubers, in contrast, showed a mixed response, exhibiting a hyper-accumulation (TF = 2.1) when treated with 11 mg F^- kg^{-1}, while for higher increasing concentrations (up to 220 mg F^- kg^{-1}) the TF ranged from 0.3 to 0.1.

Only one study assessed the impacts of AlF on the fluoride accumulation in rapeseed (25-75 mg F^- kg^{-1}) with TF ranging from 0.6 to 0.2 with a dose-dependent decreasing trend.

When fluoride was applied in the form of KF to soil (20-300 mg F^- kg^{-1}), the edible organs of triticale, narrow leaf-lupin, yellow lupin, sainfoin, radish and maize showed a TF always < 0.3.

As a well-known hyper-accumulator, the TF of the leaves of tea plants treaded with NH_4F or NaF (10-500 mg F^- kg^{-1}) reached markedly higher values compared to the TF of all the other considered species (up to 76). Only in one study the TF of tea was found to be lower than 1 (SF3 - Table 6).

In general, for almost all the crops, roots were the organs that accumulated fluoride most. An exception was represented by tea plant and Japanese camellia that, as expected, hyper-accumulated fluoride in the leaves which showed higher concentrations compared to roots and young shoots (Camarena-Rangel, et al., 2015, Ruan, et al., 2004, Yang, et al., 2016); this trend was moreover confirmed also in the previously mentioned field-scale studies (Fung, et al., 1999, Fung, et al., 2003, Ruan and Wong, 2001, Xie, et al., 2007). Another exception was represented by a study of Chen et al. (2017) on radish where the authors found that the accumulation of fluoride was highest in leaves than in roots. However, other studies conducted in radish confirmed the common higher concentration of fluoride in roots compared to leaves or, more generally, to aerial biomass (Chakrabarti and Patra, 2013a, Szostek and Ciećko, 2014). Furthermore, when mimicked sprinkler irrigation was applied (70-80% of water poured into the pot and 20-30% sprayed on plants) wheat (var. Raj. 3077) and barley (RD-2052) showed the highest concentration of fluoride in leaves, followed by stems, and then roots and grains (Agarwal and Chauhan, 2014, 2015). In other studies on cereals, roots were confirmed as the organs with the highest accumulation of fluoride, usually followed by the leaves and shoots and finally the grains (Chakrabarti, et al., 2013b, Jha, et al., 2013a, Mackowiak, et al., 2003, Szostek and Ciećko, 2014) or, in some other cases, as in the studies of Bhargava and Bhardwa (2011) on wheat (var. Raj. 4083) and Gautam and Bhardwaj (2010a) on barley (var. RD-2683), with the grains or crop ears accumulating more fluoride than shoot and leaves, respectively.

In crops as lady’s finger and sugar cane, leaves were the second organ for fluoride concentration followed by fruits and shoots (lady’s finger) or stem (sugar cane). At the opposite, in pakchoi, water spinach and lettuce, stems accumulated more fluoride than foliage (Zhang, et al., 2018). In mustard Ahmad et al. (2015) and Yadav et al. (2018) observed the following order: roots > seeds > shoots >

leaves, while Chakrabarti and Patra (2013a) found a higher concentration of fluoride in leaves than in seeds. In olive tree the pattern was: roots > shoot > leaves > fruits (Zouari, et al., 2014). In onion, after roots, the shoot accumulated more fluoride than the bulb and in slender amaranth leaves accumulated more than seeds (Jha, et al., 2009, Stanley, et al., 2002).

In many species (winter oilseed rape, narrow-leaf lupine, yellow lupine, phacelia and spinach) the accumulation pattern roots > aerial mass was observed but the partitioning among aerial organs was not investigated (Jha, et al., 2008b, Li, et al., 2018, Szostek and Ciećko, 2014). In some other cases, the accumulation pathway among organs was variable depending on the level of fluoride to which the plants were exposed (Bustingorri, et al., 2015, Bustingorri and Lavado, 2014, Das, et al., 2015).

3.3.2. Fluoride uptake

In the examined studies, an overall increasing trend of fluoride accumulation in organs of plants treated with rising concentrations of fluoride in soil or water was observed.

The highest fluoride concentration (3217 mg F^- kg^{-1} DM) was found in rice roots in case of a hydroponic experiment; this species showed a hyper-accumulation also in the shoot (395 mg F^- kg^{-1} DM) with respect to the level of fluoride to which the plants were subjected (30 mg F^- L^{-1}) (Mackowiak, et al., 2003). Tea leaves also showed a marked capacity to accumulate fluoride reaching up to 2553 mg F^- kg^{-1} DM in plants treated with 300 mg F^- kg^{-1} in soil (Yang, et al., 2016). Japanese camellia and sugar cane were also found to have high levels of fluoride in their tissues when treated with 30 mg F^- kg^{-1} of soil, up to 553 and 697 mg F^- kg^{-1} DM (Japanese camellia) and 521 and 120 mg F^- kg^{-1} DM (sugar cane) in roots and leaves, respectively. Considering its fast growth rate, sugar cane was best recommended by authors for phytoremediation purposes (Camarena-Rangel, et al., 2015). Very high concentrations were observed also by Zouari et al., (2014) in roots (up to 1070 mg kg^{-1} DM) and shoots (up to 570 mg F^- kg^{-1} DM) of olive tree treated with concentrations of fluoride in water up to 1900 mg F^- L^{-1}, and another extremely high value (1858 mg kg^{-1} DM) was observed by

Elrashidi et al. (1998) in the biomass of barley cultivated in acid soil and treated with 400 mg F^- kg^{-1}.

Concerning cereals, when plants were treated with low concentrations of fluoride the lowest value (0.9 mg F^- kg^{-1} DM) was observed in grains of wheat irrigated with 4 mg F^- L^{-1} while, among plants treated with the highest concentrations, the maximum value (54 mg F^- kg^{-1} DM) was found in grains of rice plants treated with water at 30 mg F^- L^{-1} (Bhargava and Bhardwaj, 2011, Chakrabarti, et al., 2013b).

Among the Brassicaceae, the lowest value (0.2 mg F^- kg^{-1} DM) was observed in cabbage treated with 10 mg F^- L^{-1} while the greatest (64 mg F^- kg^{-1} DM) was found in radish roots cultivated in soil with 300 mg F^- kg^{-1}. The maximum value for mustard seeds (22 mg F^- kg^{-1} DM) was found in the variety CS-14 irrigated with 75 mg F^- L^{-1}. Even they are not edible parts, it is worth noting that the shoots of winter oilseed rape and the leaves of radish reached 193 and 300 mg F^- kg^{-1} DM, respectively, when plants were grown in a soil contaminated with 1000 mg F^- kg^{-1} (Khandare and Rao, 2006, Li, et al., 2018, Szostek and Ciećko, 2014, Yadav, et al., 2018).

Regarding pulses, values in soybean ranged between 0.4 and 9.0 mg F^- kg^{-1} DM, and 2.4 and 28 mg F^- kg^{-1} DM in seeds and leaves, respectively. The concentration of fluoride in the aerial mass of narrow-leaf lupine, yellow lupine and sainfoin varied from 3 to 8, 4 to 33 and 3 to 28 mg F^- kg^{-1} DM when plants were cultivated in soils contaminated with fluoride contents from 0 to 60, 0 to 300 and 0 to 150 mg F^- kg^{-1}, respectively (Bustingorri, et al., 2015, Bustingorri and Lavado, 2014, Szostek and Ciećko, 2014).

Among the leaf-vegetables (elephant-head amaranth, slender amaranth, coriander, water spinach, lettuce and spinach) very high values were reached in spinach (up to 220 mg F^- kg^{-1} DM) treated with 800 mg F^- kg^{-1} in soil (Jha, et al., 2008b). In lettuce, water spinach, coriander and elephant-head amaranth, treated with waters from 0 to 10 mg F^- L^{-1}, the concentrations of fluoride ranged respectively between 2.0-2.8, 4.3-6.2, 4.0-16.4 and 4.0-50.0 mg F^- kg^{-1} DM (Chakrabarti and Patra, 2013a, Khandare and Rao, 2006). Quite high concentrations were observed also in other horticultural species such as for example in potato tubers (up to 21 mg F^- kg^{-1} DM), lady's finger fruits (up to 49 mg F^- kg^{-1} DM) and onion bulbs (up to 54 mg F^- kg^{-1} DM) when exposed to the highest levels of fluoride (220, 600 and 800 mg F^- kg^{-1} of soil respectively) (Das, et al., 2015, Jha, et al., 2009, Jha, et al., 2013b).

3.4. Effects of fluoride on plants

3.4.1. Effects on growth and biomass

A decrease in the total biomass of plants exposed to rising concentrations of fluoride was observed in many crops such as barley, rice, wheat, lady's finger, onion, soybean, pea, radish, spinach, triticale and olive tree (SF3 - Table 7). In contrast, Szostek and ~~Ciecko~~Ciećko (2017b) found that increasing levels of soil fluoride contamination (up to 300 mg F^- kg^{-1} of soil administered as KF) stimulated the biomass produced by radish, phacelia, narrow-leaf lupin, yellow lupin, winter oilseed rape and aerial parts of maize plants while the production of spring triticale straw and grains, maize roots, and aerial parts of lucerne was depressed (SF3 -Table 7).

Regarding yields, when soils were contaminated with NaF, dose-dependent decreases in yield of variable magnitude were observed in different crops. At maximum contamination doses of 300-450 mg F^- kg^{-1}, a reduction in yield of about 20 and 30% was observed in tea and soybean respectively. At concentration ranging from 800-1000 mg F^- kg^{-1}, yield were reduced by 20% in spinach and by 70-80% in onion and rapeseed. When fluorine was added to the soil in the form of KF triticale showed a dose-dependent decrease of up to 34% at maximum doses (200-300 mg F^- kg^{-1}) while a slight increase was observed in the roots of radish. Low NaF concentration (0.4-10 mg F^- L^{-1}) administered to lattuce and pak-choi via irrigation water led to a marked effect in terms of yield increases (up to 170 and 180%) that reached the peak at 3 mg F^- L^{-1} while in the same trial on water spinach, the yield was initially promoted and then suppressed. At higher concentrations (200-300 mg F^{-} L^{-1}) wheat and lady's finger were observed to exhibit a reduction in yield of approximately 50 and 60% respectively. In species as wheat, soybean, pea, mustard, radish, olive tree and lady’s finger some authors also observed a reduction in shoot and root length accompanied in some cases by a decrement in the number of leaves and leaf area, number of flowers, number and length of pods, number of seeds and 1000-grain weight (SF3 - Table 8).

Concerning tea plants, Yang, et al. (2016) observed that fluoride in hydroponic cultures, administered in the form of NaF, inhibited the growth of new roots and shoot tips, and coherently Pan, et al. (2020) found a reduction in root length by up to 50% in plants grown in hydroponic cultures at 16 mg F^{-} L^{-1}. In contrast, in a pot experiment Ruan, et al. (2003) observed that the growth of tea plants was not affected even at the highest level of fluoride contamination (100 mg F^{-} kg^{-1} of soil as NH_4F). Similarly, also Sharma et al. (2014) did not observe significant effects on shoot height, root length, leaf area, number of leaves, fresh leaf weight and dry leaf weight compared to control. No negative effects on the morphological parameters was also found by Camarena-Rangel et al. (2015) in a study assessing the phytoremediation efficiency in fluoride removal of Japanese camellia and sugar cane grown in hydroponic cultures with levels of fluoride up to 10 mg L^{-1}.

3.4.2. Visible symptoms

In species as onion, tip burning was observed (Jha, et al., 2009) while in wheat plants, chlorosis and necrosis symptoms were detected (Joshi and Bhardwaj, 2012). Leaf necrosis was found also by Yang et al. (2016) in tea plants treated with 300 mg F^{-} kg^{-1} of soil and visual symptoms of fluoride toxicity appeared as well in olive leaves in which necrosis was apical and/or marginal and progressively extended over the whole surface of the leaf lamina (Zouari, et al., 2014). On the other hand, Bustingorri et al. (2015) in soybean, Jha et al. (2013a, 2008b) in rice, wheat and spinach, and Ruan et al. (2003) in tea, despite a biomass reduction found in some cases, did not observe any visible injury.

3.4.3. Oxidative stress and defensive mechanisms

Superoxide dismutases (SODs) are prevalent metalloenzymes greatly involved in the immune response of living organisms. They are the first important defence enzymes within a plant cell being able to eliminate the oxidants in the cell parts affected (Ismail and Suroto, 2012), particularly toxic superoxide radicals (ROS). Biochemical changes observed in plants under fluoride stress may be related to the antioxidative defence mechanisms operating in the plant cells (Chakrabarti and Patra, 2015). The formation and accumulation of toxic oxygen species, like hydrogen peroxide (H_2O_2), lipid peroxidation (LP) and electrolyte leakage (EL) has been associated with various types of stresses (Cai, et al., 2016a). Other studies monitored the thiobarbituric acid reactive substances (TBARS) and malondialdehyde (MDA) production as markers of free radical formation in plant tissues. Moreover, under the influence of different environmental stresses, some authors reported a reduction in glutathione (GSH) (Śnioszek, et al., 2018), ascorbic acid (AA), total flavonoid (Flav) and total polyphenol content (Phe). Antioxidant enzymes like catalase (CAT), glutathione peroxidase (GPOX) and ascorbate peroxidase (APX) can catalyse the rupture of hydrogen peroxide H_2O_2.

Various authors observed an increase in SOD activity when plants were exposed to fluoride (SF3 - Table 9), but other studies showed that whereas lower fluoride concentrations stimulated the antioxidant system, higher fluoride levels caused a significant reduction of antioxidant enzyme activities with an increase of oxidative stress indicators such as H_2O_2, TBARS, LP and EL both in roots and leaves (Cai, et al., 2016a, Chakrabarti and Patra, 2015, Zouari, et al., 2017). In a study by Bustingorri et al. (2017) on soybean a significant decrease in GSH with respect to control was observed only at high fluoride concentration. Furthermore, Snioszek et al., (2018) found significant alterations in the level of AA, GSH, Flav and Phe in pea plants cultivated in contaminated soils, compared to the control plants.

Significant variations in the AA levels were also found in different vegetable species cultivated under field conditions in fluoride contaminated areas (Mondal and Gupta, 2015, Pal, et al., 2012).

3.4.4. Effects on the content of photosynthetic pigments

Total chlorophyll reduction is primarily caused by the chlorophyll collapse or inhibition of chlorophyll synthesis due to fluoride stress (Chang and Thompson, 1963). In most of the analysed studies, the chlorophyll content of fluoride-treated plants was found to decrease with respect to controls in a dose-dependent manner. In contrast, Stanley et al. (2002) found that in amaranth the chlorophyll a and b of leaf samples was not affected by fluoride. Together with the chlorophyll decline, several authors observed also a reduction in the content of carotenoids in species ~~ad~~as lady’s finger, mustard, rice and tomato (SF3 - Table 10).

Field-studies conducted on different plant species also reported a significant decrease in the chlorophyll content of most of the vegetables cultivated in the treated or fluoride-affected areas with respect to control plants (Mondal and Gupta, 2015, Pal, et al., 2012).

A reduction in photosynthetic and chlorophyll fluorescence parameters was also found by Cai et al. (2016a) in tea plants treated with fluoride doses higher than 5 mg L^{-1}. Joshi and Bhardwaj (2012) reported a modest effect of fluoride on chlorophyll b and a significant reduction in chlorophyll a in plants irrigated with increasing levels of fluoride. Furthermore, Camarena-Rangel, et al. (2015) found that the chlorophyll decrease in camellia species was manifested after 28 days for all the fluoride levels tested observing that this parameter was a better indicator of cellular integrity than others such as oxidation or wilting. Conversely, chlorophyll concentration in sugar cane plants grown in medium with 5 or 10 mg F^{-} L^{-1} was observed to increase with respect to control plants confirming the tolerance of this species to fluoride.

3.4.5. Effects on nutrients ~~balance~~uptake

Zouari et al., (2017) suggested that the increased uptake of some minerals observed in olive could be interpreted as a defence response of plants to fluoride. Szostek and ~~Ciecko~~Ciećko (2015, 2017a) observed that the soil contamination with fluorine significantly affected the concentration of calcium, magnesium and phosphorus in all the tested species (S3 - Table 11). In contrast, tea plants subjected to fluoride treatments did not show any significant alteration in the concentrations of macro and microelements (K, Ca, Mg, S, P, Fe, Mn, Zn) in leaves (Ruan, et al., 2003, 2004) (S3 - Table 11).

3.4.6. Effects on free amino acids, proline, betaine and soluble sugars contents

A common response of plants to various types of environmental stresses is the overproduction and intracellular accumulation of free amino acids such as proline and betaine (Hayat, et al., 2012). In addition to other physiological functions, in fact, proline and betaine have an adaptive role in maintaining cell turgor or osmotic balance under stress conditions and are believed to have positive effects on enzyme and membrane integrity (Ashraf and Foolad, 2007, Dar, et al., 2016, Kavi Kishor, et al., 2015). Proline is a metal chelator, a signalling molecule and an antioxidant defence molecule preventing electrolyte leakage and normalizing concentrations of ROS (Dar, et al., 2016, Hayat, et al., 2012). Soluble sugars are also considered to have an important role in improving abiotic stress tolerance of plants by mediating osmotic adjustment and acting as ROS scavengers with antioxidant function. On the other hand, various kind of environmental stresses may compromise the photosynthesis efficiency and thus, reduce the soluble sugars supply (Keunen, et al., 2013, Ruan, et al., 2003, Sharma, et al., 2020).

Concerning proline or free amino acids accumulation in response to increasing fluoride doses, various authors consistently reported an increasing trend in species as lady’s finger, mustard, potato, olive, rice and tea (S3 - Table 12). In accordance with these findings also Pal, et al. (2012) in a field-scale experiment found that the level of proline of various plant species was higher in vegetables grown under fluoride stress conditions with respect to control plants. Conversely, Mondal and Gupta (2015) found a significant reduction in free amino acid contents in different species cultivated in a fluoride-polluted area in comparison to those grown in the control area. A mixed response was observed in the accumulation of betaine in tea leaves. At 5 mg $F^- L^{-1}$, in fact, betaine levels increased by up to 28% compared to control while at higher fluoride doses, betaine slightly decreased by up to 20% at 50 mg $F^- L^{-1}$ (Cai, et al., 2016a).

As regards soluble sugars, a steady decreased with increasing fluoride concentration was observed in lady’s finger and rice while their level increased in olive and potato tubers. In potato leaves an increase of soluble sugars content was observed in the range from 11-44 mg F^- kg^{-1} whereas a reduction of those compounds was found at 110 and 220 mg F^- kg^{-1} (Ahmed, et al., 2019b, Das, et al., 2015, Zouari, et al., 2016). In field experiments various vegetable species (with the exception of spinach and cabbage), showed a decrease in soluble sugars levels when cultivated in fluoride contaminated areas (Mondal and Gupta, 2015, Pal, et al., 2012).

3.4.7. Effects on protein, nitrogen ~~forms~~, ash, fat and fibre contents

Studies that consider the effects of soil or water fluoride contamination on plant proteins or nitrogen contents are very few (Ahmed, et al., 2019b, Das, et al., 2015, Pan, et al., 2020, Saleem, et al., 2015, Szostek and Ciećko, 2017b) and, among these, just one investigated also the effects on ash, fat and fibre content (Saleem, et al., 2015). Protein or protein nitrogen content was found to significantly decrease with increasing fluoride doses in lady’s finger, in the aerial mass of winter oilseed rape, and in potato tubers and leaves (SF3 - Table 13). Szostek and Ciećko (2017b) supposed that the fluoride-induced metabolic stress may alter the protein synthesis processes and accelerate their degradation and use for catabolic processes. A reverse relationship, *id est* an increase in the protein or N-protein content was observed in tomato, in the grains of spring triticale, in roots of black radish and in the aerial mass of Lucerne (SF3 - Table 13). At field scale, Mondal and Gupta (2015) observed an increase in the protein content of the plants grown in fluoride-treated plots, compared to control plots, in many vegetable species (onion, beet, celeriac, garlic, pea, wheat, rice and mustard while in spinach, cabbage, carrot, cucumber and lentil).

As regards the total nitrogen, its content increased with increasing soil fluoride levels in spring triticale, black radish, phacelia lucerne, maize aerial mass and roots of narrow-leaf and yellow lupine. Conversely, in the aerial mass of yellow lupine, the N-total content decreased (SF3 - Table 13). Saleem, et al. (2015) observed that the ash content of two tomato varieties (Roma and Chinar) was not affected by increasing levels of soil fluoride contamination. In Chinar variety a significant reduction of fat content was found for soil fluoride concentrations above 50 mg F^- kg^{-1} while no significant effects were observed in the fibre content. At the opposite, in Roma variety, the fibre content was significantly reduced with all the treatments while the fat content was not affected (SF3 - Table 13).

3.4.8. *Further effects*

An interesting strategy to adapt and resist high concentrations of fluoride was observed by Cai, et al. (2016a) in leaves of tea plants consisting in the reduction in stomatal aperture with an increase in the epidermal hairs number. Similar results were found in young olive trees under fluoride stress, in which slight reductions of leaf relative water content (LRWC) and stomatal conductance were detected (Zouari, et al., 2016). Moreover, among the effects caused by fluoride on plants, serious damages to the ultrastructure of the cells were observed through transmission electron microscopy within a study in tea plant conducted by Li and Chen (2018).

4. Knowledge gaps and future research perspectives

At a global level ~~about~~, it is estimated that around 200 million people are ~~estimated to be~~ at risk of hazardous exposure to fluoride, including about 66 ~~of which~~million people in India and 45 million in China~~. A~~ with a high prevalence ~~was assessed~~ also found in South America and Africa (Edmunds and Smedley, 2013).

The geographical distribution of the regions in which the fluoride in the water-soil-plant system has been investigated at field-scale so far, well reflects that of the high-fluoride groundwaters already reported by several authors (Ali, et al., 2016, Amini, et al., 2008, Edmunds and Smedley, 2013, Kimambo, et al., 2019). However, the analysis of the state of the art highlights that for some areas, such as for example the African Rift Valley, where groundwaters and surface waters recorded some of the highest concentrations of fluoride ever observed (Davies, 2008, Edmunds and Smedley, 2013), the contribution of the local food and feed contaminated crops to the daily fluoride human exposure is still poorly investigated.

Regarding India, rightly the areas in which the majority of the field-scale studies were conducted are recognised to be among the most affected of the country, first among all Rajasthan, where the risk of fluorosis concerns around 11 million people in 18 districts, and after that, Andhra Pradesh and Telangana which is the second-worst affected state in India (Ali, et al., 2016).

Concerning China, endemic fluorosis has been documented almost in all provinces and the main sources of exposure are considered to be high fluoride water, pollution from coal-burning and elevated consumption of brick tea (Kimambo, et al., 2019). This explains why a so high percentage of the studies conducted in this area (six out of twelve) focus on the accumulation of fluoride in tea plant.

The contribution of fluoride contaminated foods to the fluoride daily ingestion (and related HI) depends, as well as ~~from~~on the concentration of fluoride in the food itself, also ~~from~~on the amount of contaminated food ingested (USEPA, 1992). Therefore, to truly understand the potential impacts of the fluoride contamination of cropping systems on the health of the local communities, an essential aspect is to conduct nutritional surveys among the populations living in the contaminated areas.

From the literature analyses, it was found that, even though many field-scale studies have been conducted in the polluted regions, only a few authors carried out investigations about the eating habits of the rural populations. Further efforts in this direction would be necessary, not only to determine the EDI and HI associated with the consumed crops but also to identify which crops in a specific area give the greatest contribution to the fluoride daily ingestion (Rizzu, et al., 2020).

An effective adaptation strategy in contaminated areas could be represented by the choice of those species or cultivars that, with equal yields, show the least fluoride uptake capacity and accumulation in edible organs. With regard to this, although a certain range of plant species has been considered in the investigation on the fluoride absorption and accumulation additional research would be needed to strengthen the present knowledge on the already examined species and to include more food crops species in risk assessments. Furthermore, in order to compare the accumulation behaviour of different crop species, data on fluoride concentration in plant tissues, collected in field and pot scale experiment, should be always accompanied by the information related to the water-soluble fluoride (WS-F) in soil which allows to calculate the bio-concentration factor (BCF = concentration of F in plant tissue/concentration of WS-F in soil) (Bustingorri and Lavado, 2014). Compared to the TF, in fact, the BCF, based on the WS-F, which is the bioavailable soil fluoride fraction for plants, allows to compare the accumulation behaviour of different plant species regardless of the soil factors that could influence the mobility and the adsorption of fluoride in soils. At the opposite, these factors could interact with the species bio-accumulation attitude in determining the TF.

Concerning the effects of fluoride on plant health and production, since on most of the studied species just one or few experiments were conducted, we believe that further investigation would be necessary to confirm the existing knowledge. An aspect that would be also interesting to consider is related to the effect and the interaction linked to the presence of the counterion that accompanies the F^- in the pollutant (e.g. Na^+, K^+, NH_4^+, H^+, etc.) used in the trials conducted in controlled conditions. In this regard, could be convenient, for instance, setting up control treatments in which plants are exposed at the same concentration of the counterion without being exposed to the F^- (e.g. NaCl, KCl, etc.). Finally, greater attention should be reserved to the investigation on the effects of soil or water fluoride contamination on plant proteins or nitrogen contents, which represents an important factor influencing the nutritional quality of foods.

For clarity and data manageability purposes, in the present systematic review of literature, we decided to focus our attention only on those studies that consider the effects of soil and water fluoride contamination on the fluoride plant uptake and the productivity of adult plants at the physiological maturity stage. The choice of those boundaries led to the exclusion of a great number of papers concerning the effects of fluoride on plant germination and development in early stages. Given the importance of these parameters in determining plant yields in field-conditions, and the considerable amount of literature existing on this matter, we believe that this specific topic may also deserve a proper work of studies collection and analyses to be conducted with a systematic approach.

A further significant portion of literature that was excluded in our analysis regards all those studies in which the source of contamination is represented by the airborne fluoride. From the air, in fact, fluoride can be absorbed by the plant leaves via stomata leading to a progressive accumulation over time (Baunthiyal and Ranghar, 2015, Singh, et al., 2018). Since the two types of uptake mechanisms (by roots system or via stomata) may lead to different accumulation patterns and symptoms manifestation, we believe that studies focusing on one or the other route of entry must be reviewed and analysed separately. Airborne contamination of fluoride is a relevant issue particularly in the vicinity of industrial activities such as for example phosphate fertilizer manufacturing plants, brick kilns, aluminium and zinc smelters, glass and ceramic industries, etc. (Amundson, et al., 1990, Ben Abdallah, et al., 2006, Teixeira Rossi, et al., 2016) and the concentration of fluoride in the vegetation that grows in the nearby of these activities is utilized to bio-monitor the air contamination (Elloumi, et al., 2015). Due to the conspicuous literature produced on this matter and the significance of the subject dealt, a methodical overview of the existing knowledge on this topic would be really useful to orient future investigation on the base of the current findings.

Another topic, that has not been addressed in the present study which would worth to be considered for further studies, regards the effects of the interaction of fluoride with other water or soil elements (e.g. Ca, P, Al, etc.) and variables (e.g. pH, texture, water content, etc.) on the fluoride plant uptake and accumulation and its effect on crop productivity.

Finally, a really crucial aspect on which focus the attention in future investigation concerns the development and implementation of strategies aimed to mitigate the impacts of soil and water fluoride on plant, animal and human health. Researchers and stakeholders, in facts, would greatly benefit from a comprehensive framework of information aiming to collect all the existing options already identified to reduce the contribution of food crops to the human and animal fluoride dietary intake (e.g. use of water filters and soil amendments, phytoremediation, selection of species/variety with low bioaccumulation etc.). Such an overview would enable, in facts, the investigators to have a base on which identify and pursue the most promising research lines and the stakeholders to consider a set of possible effective mitigation options to test in their specific context.

5. Conclusive remarks

~~The outcomes of this systematic review emphasized that food and feed crops cultivated in areas affected by soil and water fluoride pollution may reach levels of fluoride concentration potentially harmful to human health. A certain number of the examined studies, in fact, highlighted that the fluoride intake deriving from those foods might significantly increase the daily fluoride ingestion of individuals, contributing, together with the consumption of contaminated water, to the risk of overcoming the recommended dose and enhancing the related hazard of incurring fluorosis diseases.~~

~~However, in spite of the efforts that were already made in the assessment of crop fluoride accumulation for some contaminated areas, mostly Asia, this review suggests that further studies are needed to analyse the fluoride in food crops particularly in those regions where the environmental fluoride contamination is a serious issue and the prevalence of fluorosis is well documented, such as for example the East African Rift Valley, from which just two field-scale studies were retrieved through this review process.~~

Through the systematic literature review process, a total of 87 studies were included in this work, among field-scale, pot, and hydroponic experimental studies, regarding the impacts of soil and water fluoride pollution on the safety and the productivity of food and feed crops at a global scale.

As regards the investigation on the effects of fluoride on plant health and production, even though some efforts in this direction were already made, ~~additional research would be needed to strengthen the available evidences and confirm the current findings. Many authors observed the manifestation of~~in our opinion, additional research would be needed to strengthen the available evidence and confirm the current findings. Fluorine contamination led, in fact, to mixed results on crop yields that were suppressed or promoted, with more or less marked effects, depending on the contaminant (NaF or KF), the route of administration (directly via soil or via irrigation water), and the crop species under study. When soils were contaminated with NaF, dose-dependent yield decreases were observed in tea, soybean (up to 20-30% at 300-450 mg F$^-$ kg^{-1}), spinach (up to 20-30% at 800 mg F$^-$ kg^{-1}), onion and rapeseed (up to 70-80% at 800-1000 mg F$^-$ kg^{-1}). The administration of NaF at low concentration (0.4-10 mg F$^-$ L^{-1}) via irrigation water led to a marked effect in terms of yield increases (up to 170 and 180%) in lettuce and pak-choi (reaching the peak at 3 mg F$^-$ L^{-1}) while, in the same trial, the yield of water spinach was initially promoted and then suppressed. At higher concentrations (200-300 mg F$^-$ L^{-1}) wheat and lady's finger were observed to exhibit a reduction in yield of approximately 50% and 60% respectively. Adding fluorine to the soil in form of KF led to contrasting results: while triticale showed a dose-dependent decrease (up to 34% at 200-300 mg F$^-$ kg^{-1}), yields of yellow lupine and rapeseed increases of up to 15% and 64% respectively (at 200-300 mg F^- kg^{-1}). Less marked increases were observed on the aerial biomass of radish and maize. At 60 mg F^- kg^{-1} narrow-leaf lupine showed a yield increase by 40%.

Many authors investigated also the toxic effects of fluoride on plants which was found to induce oxidative stress, reduction in chlorophyll content, alterations in the level of proline, betaine, soluble sugars, nitrogen and macro and micronutrients. In spite of that, the manifestation of symptoms such as visible injuries, ~~decreasing~~decrease in root and shoot length ~~and yield reduction~~ was not always observed~~, also at high doses of fluoride exposure, and in some cases, the biomass production was even stimulated by increasing fluoride levels.~~ .

From the analysis of literature on controlled condition experiments, it came out that, with few exceptions~~,~~ (i.e. Japanese camellia and tea plant), plants tend to accumulate fluoride mostly in the root system ~~and this can~~ . This could represent ~~a disadvantage~~an issue mostly in the case of crops whose edible part is represented by the ~~underground organs,~~roots, such as ~~for example~~ radish~~.~~ which, for instance, was found to accumulate up to 296 mg F^- kg^{-1} DM in the Irkutsk region of Russia. Nevertheless, in most of the examined crops the accumulation of fluoride in other edible parts (e.g. leaves, fruits, tubers, bulbs, or seeds) ~~–can reach~~was found to be dose-dependent, reaching considerable levels when plants ~~are~~were exposed to ~~increasing doses of~~ high fluoride ~~–~~doses. However, as far as the non-carcinogenic chronic effects of fluoride on human health are concerned, it is not possible to give *a priori* an absolute indication on the potential hazard related to the consumption of a contaminated food product. The contribution to the fluoride daily ingestion (and related HI), depends in fact, apart from the concentration of fluoride in the food itself, also on the amount of contaminated food ingested. In this regard, to better assess the potential impacts of the fluoride contamination of cropping systems on the health of the local communities, the investigation on the eating habits of the populations living in contaminated areas is fundamental. The areas where the populations mainly practice subsistence farming and the food products are self-consumed would be in fact the most affected. Among the examined field-scale experiments, the few authors that carried out nutritional surveys among local rural populations highlighted a significant contribution of the fluoride contaminated foods to the risk of overcoming the recommended dose enhancing the hazard of incurring fluorosis diseases.

In particular, in our opinion, field studies oriented to assess the extent of the fluoride contamination in the food chain would deserve greater investigation efforts in some seriously affected regions so far neglected. In fact, the majority of the field studies that were found through our analyses were located in Asia (India ~ 42% and China ~ 32%), while very few field experiments were found for Africa and South America despite in these regions the environmental fluoride contamination is serious and well documented.

Even though, as reported above, it is not possible to associate the levels of fluoride reached by crops with a predetermined level of risk, recommendation on the choice of the species to be grown in contaminated areas can however be based on the degree of fluoride mobility from the soil to the edible plant parts which is commonly measured through the BCF.

In contaminated areas, therefore, the cultivation of crops with the lowest BCFs in the edible parts is the most advisable. On the contrary, the planting of crops such as tea and sugar cane, which have found to be strongly fluoride hyper-accumulators (BCF> 1), should be likely avoided.

Funding

This research was funded by the EU H2020 FLOWERED project [690378] “de - FLuoridation technologies for imprOving quality of WatEr and agRo - animal products along the East African Rift Valley in the context of aDaptation to climate change” coordinated by Prof. Giorgio Ghiglieri, University of Cagliari.

References

Agarwal, R. and S. Chauhan. 2014. Bioaccumulation of sodium fluoride toxicity in *Triticum aestivum* var. Raj. 3077. ~~Interantional~~International Journal of Food, Agriculture and Veterinary Sciences 4: 98-101.

Agarwal, R. and S. Chauhan. 2015. Bioaccumulation of sodium fluoride toxicity in plant parts at different phases and its impact on crop *Hordeum vulgare* (Barley) Variety RD 2052. International Journal of Multidisciplinary Research and Development 2: 16-21.

Ahmad, S., S. Ahmad, M. Ahmad, R. Shah and M. Nawaz. 2015. Bioaccumulation of fluoride ion at three flowering stages in different plant parts of mustard. Fluoride 48: 169-173.

Ahmed, S., M. Karamat, A. Haider, F. Jabeen, M.N. Ahmad, M. Ansari, et al. 2020. Ameliorative effects of salicylic acid on dry biomass and growth of *Pisum sativum* L. under sodium fluoride stress. Fluoride 53: 335-355.

Ahmed, S., K. Khalid, F. Jabeen, M. Ahmad, A. Zia, A. Haiderc, et al. 2019b. The effects of fluoride stress on Okra (*Abelmoschus esculentus* L.). Fluoride 52: 354-361.

Ahmed, S., K. Khalid, F. Jabeen, M. Ahmad, A. Zia, M. Muhajid, et al. 2019a. Productivity assessment of Okra under sodium fluoride stress. Fluoride 52: 348-353.

Ali, S., S. Thakur, A. Sarkar and S. Shekhar. 2016. Worldwide contamination of water by fluoride. Environmental Chemistry Letters 14: 291-315. doi:10.1007/s10311-016-0563-5.

Amini, M., K. Mueller, K. Abbaspour, T. Rosenberg, M. Afyuni, K. Møller, et al. 2008. Statistical modeling of global geogenic fluoride contamination in groundwaters. Environmental Science & Technology 42: 3662-3668. doi:10.1021/es071958y.

Amundson, R.G., A.J. Belsky and R.C. Dickie. 1990. Fluoride deposition via litterfall in a coastal-plain pine plantation in South Carolina. Water, Air, and Soil Pollution 50: 301-310. doi:10.1007/BF00280631.

Ashraf, M. and M. Foolad. 2007. Roles of glycine betaine and proline in improving plant abiotic stress resistance. Environmental and Experimental Botany 59: 206-216. doi:10.1016/j.envexpbot.2005.12.006.

Baunthiyal, M. and S. Ranghar. 2014. Physiological and biochemical responses of plants under fluoride stress: an overview. Fluoride 47: 287-293.

Baunthiyal, M. and S. Ranghar. 2015. Accumulation of fluoride by plants: potential for phytoremediation. Clean-Soil Air Water 43: 127-132. doi:10.1002/clen.201300353.

Begum, A., S. Harikrishna and I. Khan. 2008. Environmental fluoride level in Anekal Taluk of Bangalore District. Rasayan Journal on Chemistry 1: 774-781.

Ben Abdallah, F., N. Elloumi, I. Mezghani, J.P. Garrec and M. Boukhris. 2006. Industrial fluoride pollution of Jerbi grape leaves and the distribution of F, Ca, Mg, and P in them. Fluoride 39: 43-48.

Bharati, P., A. Kubakaddi, M. Rao and R.K. Naik. 2005. Clinical symptoms of dental and skeletal fluorosis in Gadag and Bagalkot districts of Karnataka. Journal of Human Ecology 18: 105-107. doi:10.1080/09709274.2005.11905816.

Bhargava, D. and N. Bhardwaj. 2011. Phytotoxicity of fluoride on a wheat variety (*Triticum aestivum* var. Raj. 4083) and its bioaccumulation at the reproductive phase. Asian Journal of Experimental Sciences 25: 37-40.

Bhattacharya, P., A.C. Samal, S. Banerjee, J. Pyne and S.C. Santra. 2017. Assessment of potential health risk of fluoride consumption through rice, pulses, and vegetables in addition to consumption of fluoride-contaminated drinking water of West Bengal, India. Environmental Science and Pollution Research International 24: 20300-20314. doi:10.1007/s11356-017-9649-2.

Bilotta, G.S., A.M. Milner and I. Boyd. 2014. On the use of systematic reviews to inform environmental policies. Environmental Science & Policy 42: 67-77. doi:10.1016/j.envsci.2014.05.010.

Brahman, K.D., T.G. Kazi, J.A. Baig, H.I. Afridi, A. Khan, S.S. Arain, et al. 2014. Fluoride and arsenic exposure through water and grain crops in Nagarparkar, Pakistan. Chemosphere 100: 182-189. doi:10.1016/j.chemosphere.2013.11.035.

Bustingorri, C., K. Balestrasse and R.S. Lavado. 2015. Effects of high arsenic and fluoride soil concentrations on soybean plants. Phyton 84: 407-416.

Bustingorri, C. and R.S. Lavado. 2014. Soybean as affected by high concentrations of arsenic and fluoride in irrigation water in controlled conditions. Agricultural Water Management 144: 134-139. doi:10.1016/j.agwat.2014.06.004.

Bustingorri, C., G. Noriega, R.S. Lavado and K. Balestrasse. 2017. Protective effect exerted by soil phosphorus on soybean subjected to arsenic and fluoride. Redox Report 22: 353-360. doi:10.1080/13510002.2016.1276253.

Cai, H., Y. Dong, Y. Li, D. Li, C. Peng, Z. Zhang, et al. ~~2016~~2016a. Physiological and cellular responses to fluoride stress in tea (*Camellia sinensis*) leaves. Acta Physiologiae Plantarum 38: 144. doi:10.1007/s11738-016-2156-0.

Cai, H., X. Zhu, C. Peng, W. Xu, D. Li, Y. Wang, et al. ~~2016~~2016b. Critical factors determining fluoride concentration in tea leaves produced from Anhui province, China. Ecotoxicology and Environmental Safety 131: 14-21. doi:10.1016/j.ecoenv.2016.04.023.

Camarena-Rangel, N., Á.N. Rojas-Velázquez and M. del Socorro Santos-Díaz. 2015. Fluoride bioaccumulation by hydroponic cultures of camellia (*Camellia japonica* spp.) and sugar cane (*Saccharum officinarum* spp.). Chemosphere 136: 56-62. doi:10.1016/j.chemosphere.2015.03.071.

Chakrabarti, S. and P.K. Patra. 2013a. Effect of fluoride on superoxide dismutase activity in four common crop plants. Fluoride 46: 59-62.

Chakrabarti, S. and P.K. Patra. 2015. Biochemical and antioxidant responses of paddy (*Oryza sativa* L.) to fluoride stress. Fluoride 48: 56-61.

Chakrabarti, S., P.K. Patra and B. Mondal. 2013b. Uptake of fluoride by two paddy (*Oryza sativa* L.) varieties treated with fluoride-contaminated water. Paddy and Water Environment 11: 619-623. doi:10.1007/s10333-012-0342-2.

Chen, Y., S. Wang, Z. Nan, J. Ma, F. Zang, Y. Li, et al. 2017. Effect of fluoride and cadmium stress on the uptake and translocation of fluoride and cadmium and other mineral nutrition elements in radish in single element or co-taminated sierozem. Environmental and Experimental Botany 134: 54-61. doi:10.1016/j.envexpbot.2016.11.002.

Choudhary, S., M. Rani, O.S. Devika, A. Patra, R.K. Singh and S.K. Prasad. 2019. Impact of fluoride on agriculture: A review on it's sources, toxicity in plants and mitigation strategies. International Journal of Chemical Studies 7: 1675-1680.

CMH. 2012. National food safety standards. China, The ministry of health of the People's Republic of China. China Environmental Science Press: 1-17 (Chinese).

Collaboration for Environmental Evidence. 2013. Guidelines for systematic review and evidence synthesis in environmental management. Version 4.2. Environmental Evidence, Bangor, United Kingdom.

Cronin, S.J., V. Manoharan, M.J. Hedley and P. Loganathan. 2000. Fluoride: A review of its fate, bioavailability, and risks of fluorosis in grazed-pasture systems in New Zealand. New Zealand Journal of Agricultural Research 43: 295-321. doi:10.1080/00288233.2000.9513430.

Dagnaw, L.A., B.S. Chandravanshi and F. Zewge. 2017. Fluoride content of leafy vegetables, irrigation water, and farmland soil in the Rift Valley and in non-Rift Valley areas of Ethiopia. Fluoride 5: 409-429.

Dar, M., M. Naikoo, F. Rehman, F. Naushin and F. Khan. 2016. Proline accumulation in plants: roles in stress tolerance and plant development. In: I. N, N. R and A. K. N, editors, Osmolytes and plants acclimation to changing environment: emerging omics technologies. Springer, New Delhi. p. 155-166.

Das, C., U. Dey, D. Chakraborty, J.K. Datta and N.K. Mondal. 2015. Fluoride toxicity effects in potato plant (*Solanum tuberosum* L.) grown in contaminated soils. Octa Journal of Environmental Research 3: 136-143.

Davies, T. 2008. Environmental health impacts of East African Rift volcanism. Environmental Geochemistry and Health 30: 325-338. doi:10.1007/s10653-008-9168-7.

De Troiani, R.M., T.M. Sanchez and R.S. Lavado. 1987. Soil response and alfalfa fluoride content as affected by irrigation water. Fluoride 20: 14-17.

Ding, Z., Y. Li, Q. Sun and H. Zhang. 2018. Trace Elements in Soils and Selected Agricultural Plants in the Tongling Mining Area of China. International Journal of Environmental Research and Public Health 15: 202. doi:10.3390/ijerph15020202.

Edmunds, W.M. and P.L. Smedley. 2013. Fluoride in natural waters. In: O. S. e. al., editor Essentials of Medical Geology: Revised Edition. Springer, Netherlands. p. 311-336.

Elloumi, N., M. Zouari, L. Chaari, B. Ben Rouina, F. Ben Abdallah and M. Kallel. 2015. Morphological and physiological changes induced in *Olea europaea* and *Prunus dulcis* exposed to air fluoride pollution. Brazilian Journal of Botany 38: 99-106. doi:10.1007/s40415-014-0112-z.

Elrashidi, M.A., N. Persaud and V.C. Baligar. 1998. Effect of fluoride and phosphate on yield and mineral composition of barley grown on three soils. Communications in Soil Science and Plant Analysis 29: 269-283. doi:10.1080/00103629809369945.

Fung, K.F., Z.Q. Zhang, J.W.C. Wong and M.H. Wong. 1999. Fluoride contents in tea and soil from tea plantations and the release of fluoride into tea liquor during infusion. Environmental Pollution 104: 197-205. doi:10.1016/S0269-7491(98)00187-0.

Fung, K.F., Z.Q. Zhang, J.W.C. Wong and M.H. Wong. 2003. Aluminium and fluoride concentrations of three tea varieties growing at Lantau Island, Hong Kong. Environmental Geochemistry and Health 25: 219-232. doi:10.1023/A:1023233226620.

Gautam, R. and N. Bhardwaj. 2010a. Bioaccumulation of Fluoride in Different Plant Parts of *Hordeum Vulgare* (barley) Var. Rd-2683 from Irrigation Water. Fluoride 43: 57-60.

Gautam, R., N. Bhardwaj and Y. Saini. 2010b. Fluoride accumulation by vegetables and crops grown in nawa tehsil of Nagaur District (Rajasthan, India). Journal of Phytology 2: 80-85.

Gupta, S. and S. Banerjee. 2009. Fluoride accumulation in paddy (*Oryza sativa*) irrigated with fluoride-contaminated groundwater in an endemic area of the Birbhum district, West Bengal. Fluoride 42: 224-227.

Gupta, S. and S. Banerjee. 2011. Fluoride accumulation in crops and vegetables and dietary intake in a fluoride-endemic area of West Bengal. Fluoride 44: 153-157.

Hayat, S., Q. Hayat, M. Alyemeni, A. Wani, J. Pichtel and A. Ahmad. 2012. Role of proline under changing environments: a review. Plant Signal Behav 7: 1456-1466. doi:10.4161/psb.21949.

He, L., C. Tu, S. He, J. Long, Y. Sun, Y. Sun, et al. 2020. Fluorine enrichment of vegetables and soil around an abandoned aluminium plant and its risk to human health. Environmental Geochemistry and Health 1. doi:~~https://doi.org/~~10.1007/s10653-020-00568-5.

He, X., P. Li, Y. Ji, Y. Wang, Z. Su and V. Elumalai. 2020. Groundwater Arsenic and Fluoride and Associated Arsenicosis and Fluorosis in China: Occurrence, Distribution and Management. Exposure and Health 12: 355-368. doi:10.1007/s12403-020-00347-8.

Ismail, M. and A. Suroto. 2012. Response of biochemical activities on selected rice plants towards ozone stress. International Conference on Nanotechnology and Chemical Engineering (ICNCS’2012). Bangkok, Thailand. p. 38-40.

Jezierska-Madziar, M. and P. Pinskwar. 2003. Fluoride in common reeds (*Phragmites australis*) sampled from the old Warta reservoirs near Lubon and Radzewice, Poland. Fluoride 36: 21-24.

Jha, S.K., T. Damodaran, C.L. Verma, V.K. Mishra, D.K. Sharma, V. Sah, et al. 2013a. Fluoride partitioning in rice (*Oryza sativa*) and wheat (*Triticum aestivum*) upon irrigation with fluoride-contaminated water and its risk assessment. South Asian Journal of Experimental Biology 3: 137-144.

Jha, S.K., A.K. Nayak and Y.K. Sharma. 2008b. Response of spinach (*Spinacea oleracea*) to the added fluoride in an alkaline soil. Food and Chemical Toxicology 46: 2968-2971. doi:10.1016/j.fct.2008.05.024.

Jha, S.K., A.K. Nayak and Y.K. Sharma. 2009. Fluoride toxicity effects in onion (*Allium cepa* L.) grown in contaminated soils. Chemosphere 76: 353-356. doi:10.1016/j.chemosphere.2009.03.044.

Jha, S.K., A.K. Nayak, Y.K. Sharma, V.K. Mishra and D.K. Sharma. 2008a. Fluoride accumulation in soil and vegetation in the vicinity of brick fields. Bulletin of Environmental Contamination and Toxicology 80: 369-373. doi:10.1007/s00128-008-9391-z.

Jha, S.K., Y.K. Sharma, T. Damodaran, V.K. Mishra and D.K. Sharma. 2013b. Bio-concentration of fluoride in Lady's finger (*Abelmoschus esculentus*) grown in contaminated alkaline soil and evaluation of exposure risk in human. Toxicological and Environmental Chemistry 95: 138-149. doi:10.1080/02772248.2012.745981.

Joshi, M. and N. Bhardwaj. 2012. Effect of fluoride on growth parameters and its accumulation in *Triticum Aestivum* var. Raj 3675. Fluoride 45: 297-301.

Kavi Kishor, P., P. Hima Kumari, M. Sunita and N. Sreenivasulu. 2015. Role of proline in cell wall synthesis and plant development and its implications in plant ontogeny. Frontiers in Plant Science 6: 544. doi:10.3389/fpls.2015.00544.

Kazi, T.G., H.I. Afridi, J.A. Baig and K.D. Brahman. 2019. Bioaccumulation of arsenic and fluoride in vegetables from growing media: health risk assessment among different age groups. Environmental Geochemistry and Health 41: 1223-1234. doi:10.1007/s10653-018-0207-8.

Keunen, E., D. Peshev, J. Vangronsveld, W. Van Den Ende and A. Cuypers. 2013. Plant sugars are crucial players in the oxidative challenge during abiotic stress: extending the traditional concept. Plant, Cell Environ. 36: 1242-1255. doi:10.1111/pce.12061.

Khandare, A.L. and G.S. Rao. 2006. Uptake of fluoride, aluminum and molybdenum by some vegetables from irrigation water. Journal of Human Ecology 19: 283-288. doi:10.1080/09709274.2006.11905892.

Kimambo, V., P. Bhattacharya, F. Mtalo, J. Mtamba and A. Ahmad. 2019. Fluoride occurrence in groundwater systems at global scale and status of defluoridation - State of the art. Groundwater for Sustainable Development 9: 100223. doi:j.gsd.2019.100223.

Lakshmi, D.V., K.J. Rao, T. Ramprakash and A.P.K. Reddy. 2016. Fluoride distribution in groundwater, soil and some crops grown in fluoride endemic area. Asian Journal of Environmental Science 11: 137-143.

Lakshmi, D.V., K.J. Rao, T. Ramprakash, A.P.K. Reddy and K.V. Kendra. 2017a. Bioaccumulation of fluoride in different plant parts of food crops grown in Narkatpally Mandal of Nalgonda District, Telangana. Environment & Ecology 35: 1753-1758.

Lakshmi, V.D., J.K. Rao, T. Ramprakash and A.P.K. Reddy. 2017b. Fluoride accumulation by crops grown in parts of Nalgonda District, Telangana State, India. Environment Conservation Journal 18: 79-86. doi:10.36953/ECJ.2017.181211.

Li, C. and Y. Chen. 2018. Effects of external calcium on the cell ultrastructure of tea plants under aluminium and fluoride stress. Fluoride 51: 243-251.

Li, Y., S. Wang, Z. Nan, F. Zang, H. Sun, Q. Zhang, et al. 2019. Accumulation, fractionation and health risk assessment of fluoride and heavy metals in soil-crop systems in northwest China. Science of the Total Environment 663: 307-314. doi:10.1016/j.scitotenv.2019.01.257.

Li, Y., S. Wang, D. Prete, S. Xue, Z. Nan, F. Zang, et al. 2017. Accumulation and interaction of fluoride and cadmium in the soil-wheat plant system from the wastewater irrigated soil of an oasis region in northwest China. Science of the Total Environment 595: 344-351. doi:10.1016/j.scitotenv.2017.03.288.

Li, Y., S. Wang, Q. Zhang, F. Zang, Z. Nan, H. Sun, et al. 2018. Accumulation, interaction and fractionation of fluoride and cadmium in sierozem and oilseed rape (*Brassica napus* L.) in northwest China. Plant Physiology and Biochemistry 127: 457-468. doi:10.1016/j.plaphy.2018.04.017.

Loganathan, P., M.J. Hedley, G.C. Wallace and A.H.C. Roberts. 2001. Fluoride accumulation in pasture forages and soils following long-term applications of phosphorus fertilisers. Environmental Pollution 115: 275-282. doi:10.1016/S0269-7491(01)00102-6.

Luo, J., D. Ni, C. He, S. Zhang, S. Liu, Y. Du, et al. 2019. Influence of exogenous calcium on the physiological, biochemical, phytochemical and ionic homeostasis of tea plants (*Camellia sinensis* (L.) O. Kuntze) subjected to fluorine stress. Plant Growth Regulation 87: 455-465. doi:10.1007/s10725-019-00478-2.

Mackowiak, C.L., P.R. Grossl and B.G. Bugbee. 2003. Biogeochemistry of fluoride in a plant-solution system. Journal of Environmental Quality 32: 2230-2237. doi:10.2134/jeq2003.2230.

Moeinian, K., M.R. Mehrasbi, H. Hassanzadazar, K. Kamali and E. Rabiei. 2016. Fluoride levels in soil and crops of tomato and onion farms of Zanjan. Journal of Human Environment and Health Promotion 2: 47-51. doi:10.29252/jhehp.2.1.47.

Moher, D., A. Liberati, J. Tetzlaff, D.G. Altman and T.P. Group. 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 6: e1000097. doi:~~https://doi.org/~~10.1371/journal.pmed.1000097.

Mondal, D. and S. Gupta. 2015. Influence of fluoride contaminated irrigation water on biochemical constituents of different crops and vegetables with an implication to human risk through diet. Journal of Materials and Environmental Science 6: 3134-3142.

Nagaraju, A., A. Thejaswi and J. Aitkenhead-Peterson. 2017. Fluoride and heavy metal accumulation by vegetation in the fluoride affected area of Talupula, Anantapur district, Andhra Pradesh. Journal of the Geological Society of India 89: 27-32. doi:10.1007/s12594-017-0555-5.

Okibe, F., E. Ekanem, E. Paul, G. Shallangwa, P. Ekwumemgbo, M. Sallau, et al. 2010. Fluoride content of soil and vegetables from irrigation farms on the bank of river Galma, Zaria, Nigeria. Australian Journal of Basic and Applied Sciences 4: 779-784.

Ozsvath, D.L. 2009. Fluoride and environmental health: a review. Reviews in Environmental Science and Bio/Technology 8: 59-79. doi:10.1007/s11157-008-9136-9.

Pal, K.C., N.K. Mondal, R. Bhaumik, A. Banerjee and J.K. Datta. 2012. Incorporation of fluoride in vegetation and associated biochemical changes due to fluoride contamination in water and soil: a comparative field study. Annals of Environmental Science 6: 123-139.

Pan, J., D. Li, J. Zhu, Z. Shu, X. Ye, A. Xing, et al. 2020. Aluminum relieves fluoride stress through stimulation of organic acid production in *Camellia sinensis*. ~~Physiol. Mol. Biol.~~Physiology and Molecular Biology of Plants 26: 1127-1137. doi:10.1007/s12298-020-00813-2.

Pullin, A.S. and T.M. Knight. 2009. Doing more good than harm - building an evidencebase for conservation and environmental management. Biological Conservation 142: 931- 934. doi:10.1016/j.biocon.2009.01.010.

Pullin, A.S. and G.B. Stewart. 2006. Guidelines for systematic review in conservation and environmental management Conservation Biology 20: 1647-1656. doi:10.1111/j.1523-1739.2006.00485.x.

Ranjan, S. and S. Yasmin. 2015. Assessment of fluoride intake through food chain and mapping of endemic areas of Gaya District, Bihar, India. Bulletin of Environmental Contamination and Toxicology 94: 220-224. doi:10.1007/s00128-014-1396-1.

Rizzu, M., A. Tanda, L. Canu, K. Masawe, K. Mtei, M. Deroma, et al. 2020. Fluoride uptake and translocation in food crops grown in fluoride- rich soils. Journal of the Science of Food and Agriculture 100: 5498-5509. doi:10.1002/jsfa.10601.

Ruan, J., L. Ma, Y. Shi and W. Han. 2003. Uptake of fluoride by tea plant (*Camellia sinensis* L.) and the impact of aluminium. Journal of the Science of Food and Agriculture 83: 1342-1348. doi:10.1002/jsfa.1546.

Ruan, J., L. Ma, Y. Shi and W. Han. 2004. The impact of pH and calcium on the uptake of fluoride by tea plants (*Camellia sinensis* L.). Annals of Botany 93: 97-105. doi:10.1093/aob/mch010.

Ruan, J. and M.H. Wong. 2001. Accumulation of fluoride and aluminium related to different varieties of tea plant. Environmental Geochemistry and Health 23: 53-63. doi:10.1023/A:1011082608631.

Saini, P., S. Khan, M. Baunthiyal and V. Sharma. 2013. Mapping of fluoride endemic area and assessment of F^{-1} accumulation in soil and vegetation. Environmental Monitoring and Assessment 185: 2001-2008. doi:10.1007/s10661-012-2683-0.

Saleem, M., M.N. Ahmad, B.A. Khan, A. Zia, S.S. Ahmad, H.U. Shah, et al. 2015. Effects of soil fluoride on the growth and quality of two tomato varieties grown in Peshawar, Pakistan. Fluoride 48: 174-178.

Sharma, C., R.K. Gupta, R.K. Pathak and K.K. Choudhary. 2014. Impact of fluoride and VAM fungi on growth and foliar fluoride accumulation in tea plants. Fluoride 47: 15-22.

Sharma, P., P. Arora, D. Kapoor, K. Khanna, P. Atri, R. Bali, et al. 2020. The Role of Sugars in Improving Plant Abiotic Stress Tolerance. In: M. Khan, A. Singh and P. Poór, editors, Improving Abiotic Stress Tolerance in Plants. CRC Press, Boca Raton. p. 31-48.

Sharma, V., M. Yadav and N. Kumari. 2018. Aluminium Fluoride induced changes in chlorophyll a fluorescence, antioxidants and psb A gene expression of *Brassica juncea* cultivars. Journal of Plant Interactions 13: 472-482. doi:10.1080/17429145.2018.1522001.

Singh, G., B. Kumari, G. Sinam, Kriti, N. Kumar and S. Mallick. 2018. Fluoride distribution and contamination in the water, soil and plants continuum and its remedial technologies, an Indian perspective - a review. Environmental Pollution 239: 95-108. doi:10.1016/j.envpol.2018.04.002.

Singh, J., D. Singh and S.V.S. Chauhan. 2001. Effect of sodium fluoride on growth and yield in wheat (*Triticum aestivum*). Indian Journal of Agricultural Sciences 71: 41-43.

Singh, S., J. Singh and N. Singh. 2013. Studies on the impact of fluoride toxicity on growth parameters of *Raphanus sativus* L. Indian Journal of Scientific Research 4: 61-63.

Singh, V., M.K. Gupta, P. Rajwanshi, S. Mishra, S. Srivastava, R. Srivastava, et al. 1995. Plant uptake of fluoride in irrigation water by ladyfinger (*Abelmorchus esculentus*). Food and Chemical Toxicology 33: 399-402. doi:10.1016/0278-6915(95)00005-M.

Śnioszek, M., A. Telesiński, B. Smolik and H. Zakrzewska. 2018. Effect of Fluoride and Bentonite on Biochemical Aspects of Oxidative Stress in *Pisum sativum* L. Journal of Ecological Engineering 19: 164-171. doi:10.12911/22998993/82425.

Sokolova, L.G., S.Y. Zorina and E.N. Belousova. 2019. Zonal cultivars of field crops as a reserve for the phytoremediation of fluorides polluted soils. International Journal of Phytoremediation 21: 577-582. doi:10.1080/15226514.2018.1540545.

Stanley, V.A., A. Shaleesha, P.B.K. Murthy and K.S. Pillai. 2002. Retarding fluoride accumulation in *Amaranthes viridis* through liming and implications of phosphorous treatment. Journal of Environmental Biology 23: 265-269.

Subba Rao, N., B. Ravindra and J. Wu. 2020. Geochemical and health risk evaluation of fluoride rich groundwater in Sattenapalle Region, Guntur district, Andhra Pradesh, India. Human and Ecological Risk Assessment: An International Journal 26: 2316-2348. doi:10.1080/10807039.2020.1741338.

Szostek, R. and Z. Ciećko. 2014. Content of fluorine in biomass of crops depending on soil contamination by this element. Fluoride 47: 294-306.

Szostek, R. and Z. Ciećko. 2015. Effect of soil contamination with fluorine on the content of phosphorus in biomass of crops. Journal of Elementology 20: 731-742.

Szostek, R. and Z. Ciećko. 2017a. Effect of soil contamination with fluorine on the contents of calcium and magnesium in the biomass of crop plants. Fluoride 50: 41-58.

Szostek, R. and Z. Ciećko. 2017b. Effect of soil contamination with fluorine on the yield and content of nitrogen forms in the biomass of crops. Environmental Science and Pollution Research International 24: 8588-8601. doi:10.1007/s11356-017-8523-6.

Teixeira Rossi, Z.T., E.M. de Castro, G. Carvalho Pereira, J.P.R. Alves Delfino Barbosa, G.W. de Almeida Carvalho, M.A. de Lima Silva Rossi, et al. 2016. Ecophysiological, anatomical and ultrastructural characteristics of *Vitex polygama* Cham. (Verbenaceae) submitted to different concentrations of fluoride. Acta Scientiarum Biological Sciences 38: 481-489. doi:10.4025/actascibiolsci.v38i4.31400.

USEPA. 1992. Guidelines for exposure assessment. In: EPA, editor Federal Register Notice. Washington, DC. p. 22887-22938.

Vithanage, M. and P. Bhattacharya. 2015. Fluoride in the environment: sources, distribution and defluoridation. Environmental Chemistry Letters 13: 131-147. doi:10.1007/s10311-015-0496-4.

Wang, C., Z. Yang, L. Chen, X. Yuan, Q. Liao and J. Ji. 2012. The transfer of fluorine in the soil-wheat system and the principal source of fluorine in wheat under actual field conditions. Field Crops Research 137: 163-169. doi:10.1016/j.fcr.2012.08.001.

Wei, W., S. Pang and D. Sun. 2019. The pathogenesis of endemic fluorosis: Research progress in the last 5 years. J. Cell. Mol. Med. 23: 2333-2342. doi:10.1111/jcmm.14185.

WHO. 1999. World Health Organization. Guidelines for drinking-water quality. Vol 2. 2nd ed. World Health Organization, Geneva.

WHO. 2011. World Health Organization. Guidelines for drinking-water quality. 4th ed. World Health Organization, Geneva.

Wu, J. and Z. Sun. 2016. Evaluation of Shallow Groundwater Contamination and Associated Human Health Risk in an Alluvial Plain Impacted by Agricultural and Industrial Activities, Mid-west China. Exposure and Health 8: 311-329. doi:10.1007/s12403-015-0170-x.

Xie, Z., Z. Chen, W. Sun, X. Guo, B. Yin and J. Wang. 2007. Distribution of Aluminum and Fluoride in Tea Plant and Soil of Tea Garden in Central and Southwest China. Chinese Geographical Science 17: 376-382. doi:10.1007/s11769-007-0376-3.

Yadav, M., N. Kumari and V. Sharma. 2018. Phytoremediation efficiency of *Brassica juncea* cultivars at vegetative and reproductive growth stages under individual and combined treatment of fluoride and aluminium. International Journal of Phytoremediation 20: 922-929. doi:10.1080/15226514.2018.1448361.

Yadav, R.K., S. Sharma, M. Bansal, A. Singh, V. Panday and R. Maheshwari. 2012. Effects of fluoride accumulation on growth of vegetables and crops in Dausa district, Rajasthan, India. Advances in Bioresearch 3: 14-16.

Yadu, B., V. Chandrakar and S. Keshavkant. 2016. Responses of plants to fluoride: an overview of oxidative stress and defense mechanisms. Fluoride 49: 293-302.

Yang, Y., Y. Liu, C.-F. Huang, J. de Silva and F.-J. Zhao. 2016. Aluminium alleviates fluoride toxicity in tea (*Camellia sinensis*). Plant and Soil 402: 179-190. doi:10.1007/s11104-015-2787-8.

Yu, L., J. Zhang, C. Du, H. Yang and B.-C. Ye. 2018. Distribution and pollution evaluation of fluoride in a soil–water–plant system in Shihezi, Xinjiang, China. Human and Ecological Risk Assessment 24: 445-455. doi:10.1080/10807039.2017.1385386.

Zhang, J., L. Yu, H. Yang and B.-C. Ye. 2018. Migration and transformation of fluoride through fluoride-containing water for the irrigation of a soil–plant system. Human and Ecological Risk Assessment 25: 1048-1058. doi:10.1080/10807039.2018.1460577.

Zhao, S., Y. Liu, J. Ma, H. Mao, T. Lan, Y. Jiang, et al. 2015. Influence of fertilizers on fluoride accumulation in tea leaves and its remediation using polyphenol-Ce adsorbents. Rsc Advances 5: 6085-6091. doi:10.1039/C4RA10361K.

Zheng, D. and L. Sun. 2011. Fluorine contents in crops and water and its health risks assessment in Liaohe River Basin, China. 2011 International Symposium on Water Resource and Environmental Protection. IEEE. p. 2314-2316.

~~Zhonglei, X., C. Zhuo, S. Wentian, G. Xiaojing, Y. Bo and W. Jinghua. 2007. Distribution of Aluminum and Fluoride in Tea Plant and Soil of Tea Garden in Central and Southwest China. Chinese Geographical Science 17: 376-382.~~

Zouari, M., C. Ben Ahmed, N. Elloumi, B. Ben Rouina, P. Labrousse and F. Ben Abdallah. 2016. Effects of Irrigation Water Fluoride on Relative Water Content, Photosynthetic Activity, and Proline Accumulation in Young Olive Trees (*Olea europaea* L. cv Chemlali) in Arid Zones. Fluoride 49: 366-372.

Zouari, M., C. Ben Ahmed, R. Fourati, D. Delmail, B. Ben Rouina, P. Labrousse, et al. 2014. Soil fluoride spiking effects on olive trees (*Olea europaea* L. cv. Chemlali). Ecotoxicology and Environmental Safety 108: 78-83. doi:10.1016/j.ecoenv.2014.06.022.

Zouari, M., N. Elloumi, K. Bellassoued, C. Ben Ahmed, M. Krayem, D. Delmail, et al. 2017. Enzymatic antioxidant responses and mineral status in roots and leaves of olive plants subjected to fluoride stress. South African Journal of Botany 111: 44-49. doi:10.1016/j.sajb.2017.03.039.

Figure legends

Supplemental Files

Supplemental File 1 (SF1) - Review Protocol

Supplemental File 2 (SF2) - List of publications included in the Systematic Review

Supplemental File 3 (SF3) - Over-sized Tables

Table 1 - Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
Every kind of study assessing: ▪ the effects of soil and water fluoride on quali-quantitative characteristics of crop production ▪ fluorine uptake capacity of different kind of crops cultivated in soils and/or irrigated with water characterized by various levels of fluoride ▪ articles focusing only on adults plants ▪ microcosm, mesocosm and field-scale trials	First and second stages (screening title and abstract): ▪ Not on topic (misclassified) ▪ No relevant population (e.g. animals, humans, seedlings) ▪ No relevant exposure (e.g. airborne contamination) ▪ Methodological articles (e.g. procedures for determination of fluoride in soil or plant material) ▪ Full text not available ▪ Not in English Third stage (assessing full text): ▪ Same criteria of the first and second stages ▪ No relevant outcome ▪ Other reasons

Table 2 - Qualitative information extracted from the studies

Variable	**Description**
Country	Country where the study was conducted
Zone	Specific study area (village or town, city, district, province etc.)
Type of experiment	Pot/Field/Hydroponic (P/F/H)
Growing conditions	Greenhouse/Open field/Growth Chamber (G/O/GC)
Source of Exposure	Soil/Water (S/W)
Pollutant	Natural pollution, NaF, KF, NH_4F etc.
Other factors and levels	Other factors considered in the cases of factorial experiments and respective levels
Fertilization or amendment management	Type and doses of fertilizers/amendments applied
Species of plant	Scientific name of the studied plants
Variety	Varieties of the studied plants, if available
Phenology stage	Phenology stage at which plant where harvested
Accumulation pathway	Fluoride accumulation pathway among different plant organs
Effects of fluoride on plants	Visible injuries, oxidative stress, enzymatic activity etc.

Table 3 - Quantitative information extracted from the studies

Kind of information extracted	**Description**
Sample size	Number of replicates per each treatment
Levels of fluoride exposure	Different levels of concentration of fluoride in water or soil
Levels of fluoride in different plant tissues	Different levels of concentration of fluoride in different plant parts (roots, stem, leaves, fruits, seeds etc.)
Yield of different plant parts	Dry matter of different plant parts or the entire plant biomass
Morphological traits	Morphological traits of the considered plant species (plant height, trunk diameter, leaf area, shoot length, root length, pod length, ear length, n. of leaves, n. of branches, n. of tillers, n. of ears, n. of flowers, n. of pods, n. of seeds, n. of seed pod^{-1}, n. of flowers ear^{-1}etc.)
Oxidative stress indicators	Oxidative stress indicators (H_2O_2: hydrogen peroxide, LP: lipid peroxidation, EL: electrolyte leakage, TBARS: thiobarbituric acid reactive substances, MDA: malondialdehyde, GSH: glutathione, AA: ascorbic acid, Flav: total flavonoid, Phe: total polyphenol content)
Antioxidant enzymes activity	Activity of the antioxidant enzymes (SOD: superoxide dismutase, CAT: catalase, GPOX: glutathione peroxidase and APX: ascorbate peroxidase)
Content of photosynthetic pigments	Content of photosynthetic pigments (chlorophyll a, chlorophyll b, carotenoids)
Nutrients uptake	Uptake rates of different nutrient elements (P, Ca, Mg, K, Al, S, Zn, Fe)
Content of free amino acids, proline, betaine and soluble sugars	Content of free amino acids, proline, betaine and soluble sugars
Content of protein, nitrogen ~~forms~~, ash, fat and fibre	Content of protein, nitrogen forms (total nitrogen, protein nitrogen, nitrate nitrogen), ash, fat and fibre

Table 4 - Number of studies collected per each category of experiment type and kind of extractable data.

Type of experiments conducted in the included studies	**N. of studies that reported data exclusively on F accumulation**	**N. of studies that reported data or results exclusively on the effects of F on plants**	**N. of studies that reported both kind of data**
Field-scale	34	2	3
Pot	10	10	19
Hydroponic	0	2	4
Field + Pot	1	0	0
Field + Hydroponic	1	0	0
Pot + Hydroponic	0	0	1

Figure 1

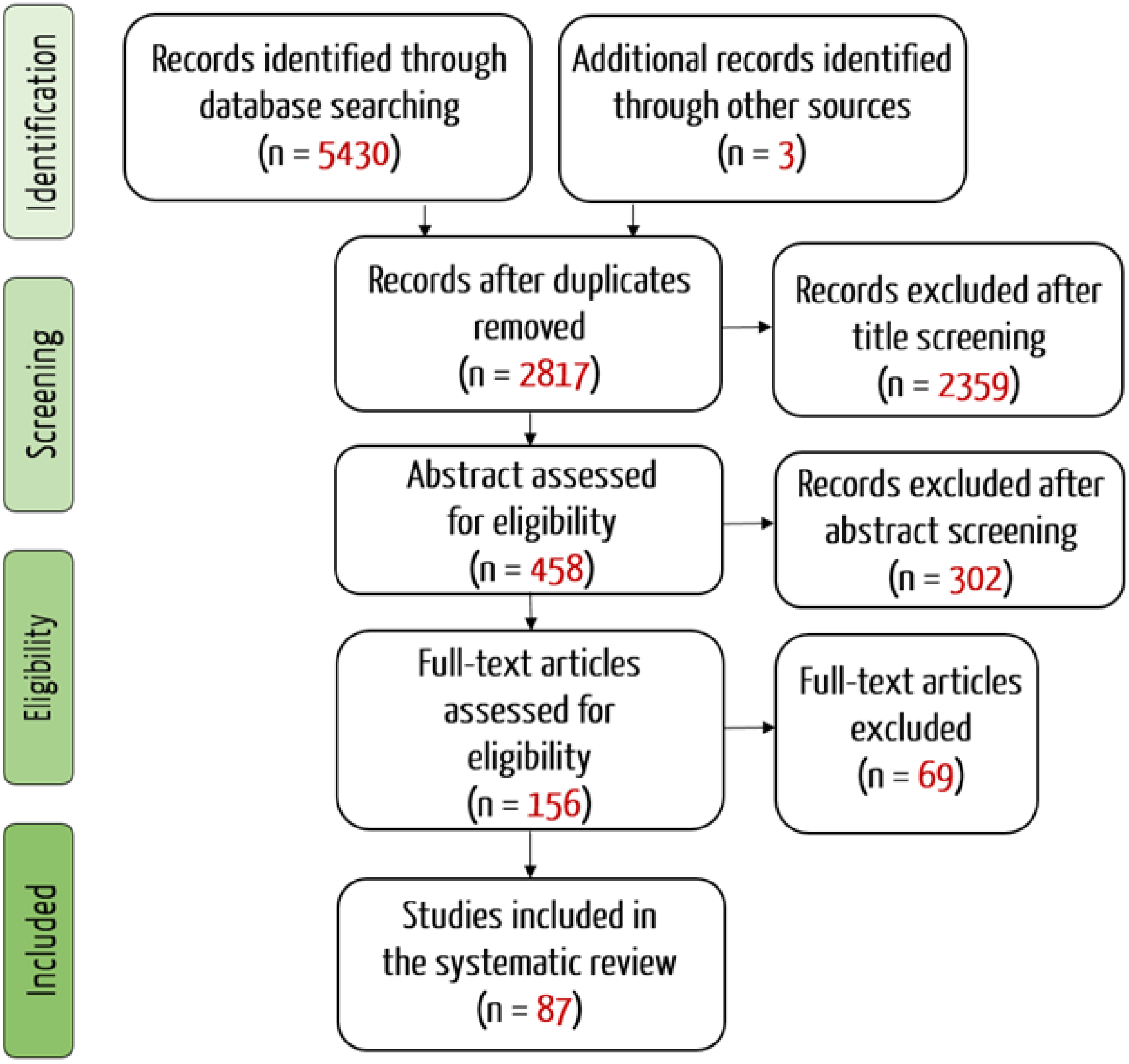
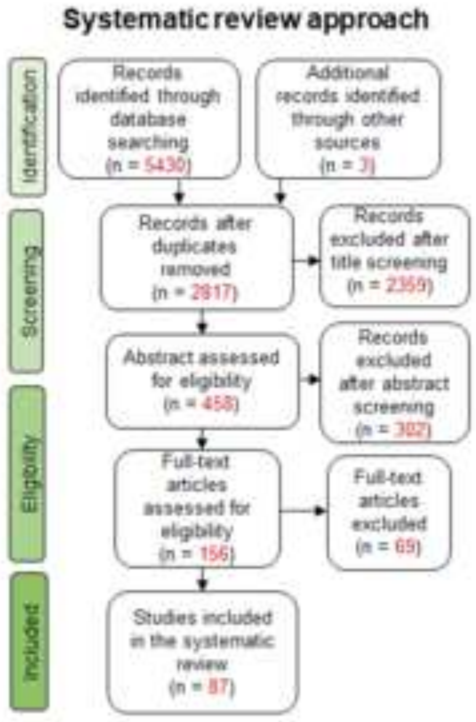

Identification
Screening
Eligibility
Included
Records identified through database searching (n = 5430)
Additional records identified through other sources (n = 3)
Records after duplicates removed (n = 2817)
Records excluded after title screening (n = 2359)
Abstract assessed for eligibility (n = 458)
Records excluded after abstract screening (n = 302)
Full-text articles assessed for eligibility (n = 156)
Full-text articles excluded (n = 69)
Studies included in the systematic review (n = 87)

Figure 2

Graphical Abstract rev1



Systematic review approach

Identification

Records identified through database searching (n = 5430)

Additional records identified through other sources (n = 3)

Screening

Records after duplicates removed (n = 2817)

Records excluded after title screening (n = 2359)

Abstract assessed for eligibility (n = 458)

Records excluded after abstract screening (n = 302)

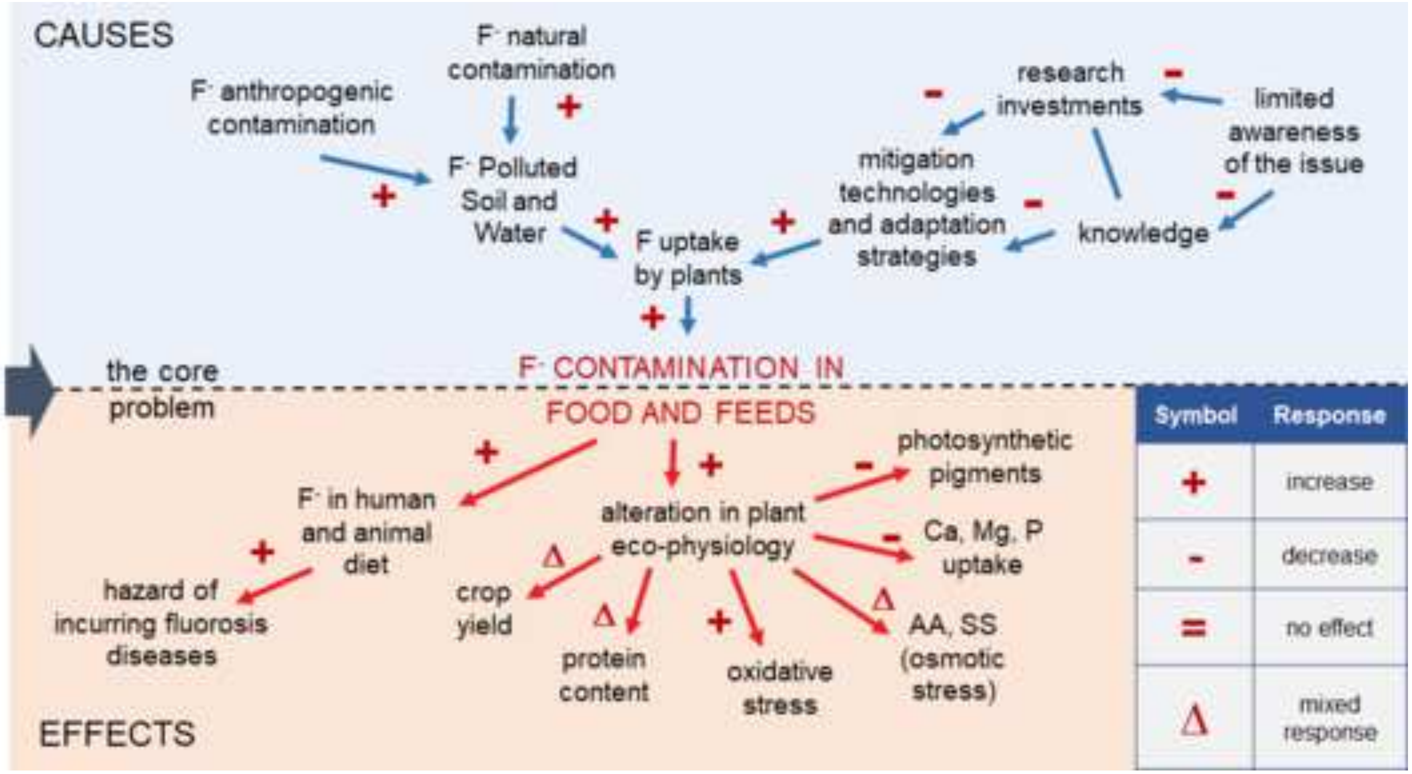
Eligibility

Full-text articles assessed for eligibility (n = 156)

Full-text articles excluded (n = 69)

Included

Studies included in the systematic review (n = 87)



CAUSES

F⁻ natural contamination

F⁻ anthropogenic contamination

F⁻ Polluted Soil and Water

F⁻ uptake by plants

research investments

limited awareness of the issue

mitigation technologies and adaptation strategies

knowledge

the core problem

F⁻ CONTAMINATION IN FOOD AND FEEDS

F⁻ in human and animal diet

hazard of incurring fluorosis diseases

alteration in plant eco-physiology

photosynthetic pigments

Ca, Mg, P uptake

crop yield

protein content

oxidative stress

AA, SS (osmotic stress)

EFFECTS

Symbol	Response
+	increase
-	decrease
=	no effect
Δ	mixed response

Highlights

1. Plants tend to accumulate fluoride mostly in the root system
2. Accumulation of F in plant tissues is dose-dependent with some exceptions
3. F contamination of food crops can represents an actual health hazard in polluted areas
4. F can alter chlorophyll levels, plant physiology and can induce oxidative stress
5. Evidences of F affecting crop yields are often contradictory even at high F levels

Impacts of soil and water fluoride contamination on the safety and productivity of food and feed crops: A systematic review

Margherita Rizzu [a,b,*], Alberto Tanda[a,b], Chiara Cappai[a,b], Pier Paolo Roggero[a,b], Giovanna Seddaiu[a,b]

[a] Dipartimento di Agraria, University of Sassari, Viale Italia 39, 07100, Sassari, Italy

[b] Desertification Research Centre, NRD, University of Sassari, Viale Italia 39, 07100, Sassari, Italy

mrizzu@uniss.it, tandaalberto@gmail.com, ccappai@uniss.it, pproggero@uniss.it, gseddaiu@uniss.it.

*Corresponding author: Margherita Rizzu

Tel.: +39 3454034148

E-mail: mrizzu@uniss.it

Address: Viale Italia 39, 07100, Sassari, Italy;

CRediT author statement:

Margherita Rizzu: Conceptualization, Methodology, Investigation, Data Curation, Writing - Original Draft preparation, Visualization. Alberto Tanda: Investigation, Data Curation, Writing- Original draft preparation. Chiara Cappai: Investigation, Draft preparation. Pier Paolo Roggero: Writing - Reviewing and Editing, Supervision. Giovanna Seddaiu: Conceptualization, Writing - Reviewing and Editing, Supervision, Resources and project management.

Abstract

Although a strong connection between the environmental fluoride contamination and the fluorosis disease is nowadays worldwide well documented, the knowledge on the fluoride contamination levels of cultivated crops at the basis of the human food-chain is limited and fragmented. Adopting a systematic approach, this study reviews the available literature concerning the impacts of soil and water fluoride pollution on the safety and productivity of food and feed crops at a global scale, with the aim to provide a comprehensive overview of the current state of the art. The analyses of literature highlighted that food and feed crops exposed to soil and water fluoride pollution may reach concentrations of fluoride potentially harmful to human health. Nevertheless, despite the efforts already made to assess the crop fluoride accumulation in contaminated areas of India and China, the present study brings to light the lack of knowledge still existing on this issue for some regions strongly affected by environmental fluoride contamination such as the East African Rift Valley. Concerning the impacts of fluoride on cultivated crops, many authors observed that fluoride can produce toxic effects on plants leading to oxidative stress, reduction in chlorophyll content, alterations in the levels of proline, betaine, soluble sugars, nitrogen and macro and micronutrients. However, the appearance of symptoms such as visible injuries, reduced root and shoot length and yield decline was not always observed, also at high levels of fluoride exposure, and in some cases, the biomass production was even stimulated by increasing fluoride doses.

Keywords: pollution, yield reduction, oxidative stress, risk assessment, hazard index, fluorosis.

1. Introduction

The association between excessive environmental fluoride occurrence and the high rate of fluorosis in the populations of polluted areas is nowadays well recognized (He, et al., 2020, Ozsvath, 2009, Subba Rao, et al., 2020, Wu and Sun, 2016). The prolonged exposure to high fluoride doses can lead, in fact, to a series of major illnesses that involve the dental apparatus and skeletal system but also, as recently examined, non-skeletal tissues as internal organs, nervous, reproductive and immune systems (Wei, et al., 2019). Although low-fluoride intakes have been recognised to have positive effects on the prevention of dental caries, moderate chronic ingestion, particularly during childhood, is known to provoke the appearance of black spots on teeth and in most severe cases their loss. Skeletal system disorders appear with the protracted intake of high fluoride doses with symptoms that comprise bone deformities, ligaments calcification and associated back, knee, shoulder and neck pain with difficulties in movements and in proper walking (Bharati, et al., 2005, WHO, 1999, 2011).

Endemic fluorosis is prevalent in at least 25 countries with the highest incidence in India, China and various African regions (Vithanage and Bhattacharya, 2015), but groundwater with concentrations above the WHO guideline limit for drinking-water (1.5 mg L^{-1}) have been found in many parts of the world. Beyond China and India, affected regions are Sri Lanka, North and West African countries (Tunisia, Libya, Sudan, Senegal, Ghana, Ivory Coast), the East African Rift Valley (Kenya, Tanzania, Ethiopia, Uganda and Rwanda), South Africa, central Argentina, northern Mexico and Pakistan (Edmunds and Smedley, 2013).

The sources of fluoride contamination can be both natural and anthropogenic with the firsts being paramount (Amini, et al., 2008). Natural sources are related to geogenic processes that are primarily responsible for groundwater pollution, such as the weathering of F-rich minerals and the release of fluoride due to volcanic activities, fumarolic gases, hydro-geothermal vents and marine aerosols. Contamination from anthropogenic activities can be significant on a local scale and may be either of industrial origin, such as the release of wastes from aluminium smelters, effluents from coal-based power stations and factories processing various materials (e.g glass, ceramic, plastics, pesticides, disinfectants, etc.), or agricultural-related such as the long-term uncontrolled use of phosphatic fertilizer or the irrigation with fluoride-enriched water (Ali, et al., 2016, Kimambo, et al., 2019, Singh, et al., 2018)

Through the polluted soil, water, and air, fluoride can enter the food-chain (Vithanage and Bhattacharya, 2015). After drinking water, in fact, the consumption of contaminated food products is considered another important source of fluoride exposure for human organisms (Brahman, et al., 2014, WHO, 2011). Furthermore, the contamination of the plant growth environment can lead to the manifestation of toxic effects in food crops with consequent yield and nutritional quality reduction and related economic losses (Ahmed, et al., 2019a, Bustingorri and Lavado, 2014).

Several field-scale explorative trials and controlled experiments have been conducted in various contaminated regions of the world to investigate the accumulation of fluoride in crops and the effects on their productivity, nevertheless, the information is still fragmented. Even though, in fact, numerous studies have considered and examined the worldwide environmental fluoride occurrence, particularly in groundwater systems (Amini, et al., 2008, Edmunds and Smedley, 2013, Kimambo, et al., 2019, Vithanage and Bhattacharya, 2015), and various overviews have been conducted on fluoride toxicity in plants (Baunthiyal and Ranghar, 2014, Baunthiyal and Ranghar, 2015, Choudhary, et al., 2019, Singh, et al., 2018, Yadu, et al., 2016), no systematic reviews have been performed concerning the impacts of soil and water fluoride pollution on the safety and the productivity of food and feed crops at a global scale.

With the aim to provide a comprehensive overview on this topic and bring to light the gaps of knowledge, this work attempted to gather all the existing scientific literature on the impacts of the environmental fluoride pollution on crop productivity and safety.

The findings of this review are intended to suggest future research directions to scientists toward a better understanding of the relationships between fluoride contamination and food safety and production as well as informing the development of possible mitigation and adaptation strategies in the affected areas.

2. Review methods

The systematic literature review followed the methodological approach reported by existing guidelines (Bilotta, et al., 2014, Collaboration for Environmental Evidence, 2013, Pullin and Knight, 2009, Pullin and Stewart, 2006). A review protocol was implemented defining the connotations of the systematic literature search, the inclusion/exclusion criteria and the data extraction forms (Supplemental File 1 - SF1).

2.1. Resources

Academic search engines such as ISI Web of Science (Web of Science Core Collection plus other databases such as Bioabs, Kjd, Medline, Rsci, Scielo), PubMed, Scopus, Science Direct, JSTOR, Agricola, Fluorideresearch.org and Cab Abstracts were used. Advanced search options were considered entering the following keywords: *fluoride OR fluorine*, in the title field, *AND crop OR plant OR vegetation OR grasses OR vegetables OR agriculture*, in the other fields. The search was restricted to the English language, and the timespan went from 1985 to 2020. To refine the results, the search conducted on the Web of Science Core Collection and the Scopus database was limited to the following subject areas:

- for the Web of Science Core Collection: *Environmental sciences, Toxicology, Water resources, Plant sciences, Soil science, Agronomy, Ecology, Agriculture multidisciplinary, Multidisciplinary sciences, Biology, Forestry, Horticulture Agricultural engineering, Physiology, Agriculture dairy animal science, Environmental studies*
- for the Scopus database: *Environmental Science, Agricultural and Biological Sciences, Multidisciplinary, Decision Sciences*

2.2. Review process

Records were stored in a reference manager software database and duplicates were eliminated. The article screening was performed following a stepwise process according to the established inclusion criteria (Table 1). A first selection was conducted on the basis of the publication title, in the second stage abstracts were assessed and finally, the remaining articles were filtered revising the whole paper. In case of doubts about the pertinence of a record, this was included and further evaluated in the next stage. A subset of the references was revised by two further independent reviewers in order to assess the reliability of the application of the inclusion criteria. The final numbers of articles recovered, duplicated, accepted and excluded were annotated to produce an accurate PRISMA flow diagram (Preferred Reporting Items for Systematic reviews and Meta-Analyses) (Moher, et al., 2009). The list of the papers that were finally included is reported in the Supplemental File 2 (SF2).

2.3. Data extraction and analysis

From the final subset of articles, available qualitative (Table 2) and quantitative (Table 3) information was extracted. If the data were not reported in the text, they were extracted from tables and graphs.

For each extracted variable, the percentages increase/decrease (Δ%) from control values to those of treated subjects were calculated and data were summarized in Tables 5-13 included in Supplemental File 3 (SF3).

In Table 6 (SF3), the Transfer Factor (TF) in the edible parts was calculated by the ratio between the concentration of fluoride of the edible organs and the concentration of total fluoride in the soil (Ding, et al., 2018). Furthermore, the accumulation pattern was reported. The TF index allows to assess the accumulation trend in plant tissues of crops subjected at increasing doses of contaminant. When TF >1, the concentration of fluoride in the plant tissues is higher than the concentration of total fluoride in soil, indicating a hyper-accumulator behaviour in the considered plant organ.

3. Results

3.1. Characteristics of the studies included in the systematic review

A total of 87 studies was retrieved through the process of the systematic review (Figure 1), with 77 % of the collected articles published after or in the year 2010.

Field-scale studies, pot experiments, hydroponic experiments and multi-experiments studies were found. Some of them reported exclusively data on fluoride accumulation in crops, from others it was possible to get only data on the effects of fluoride on plants and further articles included both types of data (Table 4).

Around 46 % of the studies were focused on soil pollution, 37 % on water pollution and the remaining 17 % on both sources of fluoride contamination.

Among the studies conducted under controlled conditions (pot and hydroponic experiments), in the 74% of the cases, NaF was used as a pollutant to contaminate the source of exposure (soil or water), KF was used in the 11% of the studies, NH_4F in another 11% while AlF and HF in the 4%.

3.2. Fluoride in the water-soil-plant system of different areas of the world and human health hazard

The areas in which the greatest number of studies has been conducted were India (~42%, 16 studies) and China (~32%, 12 studies), where the considered environmental fluoride contamination was mostly of natural origin. Concerning the other regions, just two field-scale studies (~5%) were found for Pakistan and one field-scale study (~3%) for each of the following regions was found: Argentina, Ethiopia, Iran, Nigeria, New Zealand, Poland, Russia and Tanzania (Figure 2).

Concerning India, the majority of the studies regarded the areas of Rajasthan and West Bengal, furthermore, other experiments were conducted also in Andhra Pradesh, Telangana, Bangalore, Uttar Pradesh and Bihar (SF3 - Table 5). In general, the different studies considered a wide variety of food crops, including grain crops, pulses, horticultural crops, leafy vegetables and tubers. The lowest value of soil total fluoride concentration (6.7 mg F^- kg^{-1}) was found by Nagaraju et al. (2017) in Talupula, Anantapur District, Andhra Pradesh while the highest (681.0 mg F^- kg^{-1}) was detected in Rajasthan by Saini et al. (2013). The soil water-soluble fluoride varied from 0.3 mg F^- kg^{-1} (Lakshmi, et al., 2016) in Aatmakoor Mandal, Nalgonda district, Telangana, to 73.9 mg F^- kg^{-1} in Rajasthan (Saini, et al., 2013). Concerning groundwater, the fluoride concentration ranged from 0.3 mg F^- L^{-1} in Birbhum district to 21.5 mg F^- L^{-1} in Bangalore (Begum, et al., 2008, Mondal and Gupta, 2015). The lowest contents of fluoride in various vegetable species (< 4.2 mg F^- kg^{-1} DM) were observed in the regions of Nowapara and Junidpur, Birbhum district and in Nalgonda district, Telangana (Lakshmi, et al., 2016, 2017a, 2017b, Pal, et al., 2012), while the greatest value was recorded in *Brassica oleracea* L. (296 mg F^- kg^{-1} DM) by Begum et al. (2008) in Bangalore.

Regarding China, six out of twelve field-scale studies concerned the uptake and accumulation of fluoride in tea plant (*Camellia sinensis* (L.) O. Kuntze) which is well known to be one among the fluoride hyper-accumulator species (Cronin, et al., 2000). The concentration of fluoride in young tea leaves varied from a minimum of 49.0 mg F^- kg^{-1} DM found by Xie, et al. (2007), up to 808.0 mg F^- kg^{-1} DM observed by Fung et al. (1999) in Guangdong province. Mature leaves were found to have higher concentrations compared to young ones, ranging from 221.0 mg F^- kg^{-1} DM (Xie, et al., 2007) to 2919.0 mg F^- kg^{-1} DM in Lantau Peak of Lantau Island (Fung, et al., 2003). The fluoride accumulation in edible parts of various food crops observed by different authors in China ranged from a value of 0.1 mg F^- kg^{-1} DM in cabbage up to 34.7 mg F^- kg^{-1} DM in pumpkins leaves (He, et al., 2020), and the concentration of fluoride in wheat grains (0.6-7.2 mg F^- kg^{-1} DM) was found, in most of the cases, to be higher than the national edible health standard of China (CMH, 2012) ($\leq$ 1.5 mg kg^{-1}) (Li, et al., 2019a, Li, et al., 2017, Wang, et al., 2012, Yu, et al., 2018, Zheng and Sun, 2011). Higher concentrations were found in roots, leaves and straw of wheat grown in the region of Baiyin, Gansu province and Yangtze River outfall region and in roots and leaves of maize, with the greatest value (542 mg F^- kg^{-1} DM) observed in Gansu province in roots (Li, et al., 2019a, Li, et al., 2017, Wang, et al., 2012). In this area also the highest concentration of fluoride were recorded both in soil (total fluoride: 4987 mg F^- kg^{-1}; water-soluble fluoride: 59 mg F^- kg^{-1}) and water (82 mg F^- L^{-1}) (Li, et al., 2017). The lowest values of soil total fluoride (82 mg F^- kg^{-1}) and water fluoride (0.2 mg F^- L^{-1}) were observed in Shihezi, Xinjiang by Yu et al. (2018) while the minimum soil water-soluble fluoride (0.04 mg F^- kg^{-1}) was found by Ruan and Wong (2001) in Jintan County (Jiangsu Province). Environmental fluoride pollution of natural origin was also found in the water-soil-plant systems of Argentina, Ethiopia, Nigeria, Pakistan and Tanzania (Brahman, et al., 2014, Dagnaw, et al., 2017, De Troiani, et al., 1987, Kazi, et al., 2019, Okibe, et al., 2010, Rizzu, et al., 2020), while anthropogenic sources of fluoride contamination were identified in Poland, New Zealand and Russia. In Poland, the old Warta reservoir near the town of Luboń was severely contaminated by the wastes from a nearby chemical plant (Jezierska-Madziar and Pinskwar, 2003), in New Zealand Loganathan et al. (2001) studied the effects of the long-term application of P-fertilizer on the top-soil fluoride concentration (SF3 - Table 5) while in Russia Sokolova et al. (2019) studied the effects of fluoride contaminated soils 0.5 km from the IrkAZ (one of the largest enterprises in aluminium industry in Russia) on the productivity and fluoride uptake of some field crops.

Some of the abovementioned authors, as well as assessing the fluoride accumulation in food crops also conducted nutritional surveys among the populations of the contaminated areas in order to estimate a hypothetical fluoride daily ingestion (estimated daily intake, EDI) associated with the consumption of the studied crops and the related hazard index (HI) which represents how many times the effective intake exceeds the recommended dose. In many cases, the cumulative EDI from the diet and drinking water exceeded the recommended value (HI > 1) with children and teenagers being the categories considered at major risk (Bhattacharya, et al., 2017, Brahman, et al., 2014, He, et al., 2020, Jha, et al., 2008a, Kazi, et al., 2019, Rizzu, et al., 2020).

3.3. Fluoride uptake and partitioning under controlled conditions

Among the analysed publications concerning pot and hydroponic experiments, it was possible to get data on fluoride accumulation in plant tissues of 31 different species including cereals (*Hordeum vulgare* L., *Oryza sativa* L., *x Triticosecale* Wittm., *Triticum aestivum* L., *Zea mays* L.), pseudo-cereals (*Amaranthus gangeticus* L., *Amaranthus viridis* L.), pulses (*Glycine max* L. Merrill, *Lupinus angustifolius* L., *Lupinus luteus* L., *Medicago sativa* L., *Onobrychis viciifolia* Scop., *Pisum sativum* L.), horticultural species (*Abelmoschus esculentus* (L.) Moench, *Allium cepa* L., *Coriandrum sativum* L., *Ipomoea aquatica* Forssk., *Lactuca sativa* L., *Spinacea oleracea* L.), in particular species belonging to the Brassicaceae (*Brassica chinensis* L., *Brassica juncea* L., *Brassica napus* L., *Brassica oleracea* L., *Raphanus sativus* L.) and Solanaceae families (*Lycopersicon esculentum* L., *Solanum tuberosum* L.) and further cultivated species (*Camellia japonica* L., *Camellia sinensis* (L.) O. Kuntze, *Olea europaea* L., *Phacelia spp*. Juss., *Saccharum officinarum* L.) (SF3 - Table 6).

3.3.1. Fluoride Transfer Factor (TF) in edible parts and accumulation pattern

An overall decreasing trend in the TF (which remains always < 0.4) calculated for edible parts of lady's finger, onion, radish and soybean was observed in several studies where plants were treated with increasing doses of NaF in soil (20-1000 mg F^- kg^{-1}). A decreasing behaviour was observed also in the case of spinach (50-800 mg F^- kg^{-1}) with TF of leaves reaching higher values (1-0.5) at the lowest concentrations (< 200 mg F^- kg^{-1}). Potato tubers, in contrast, showed a mixed response, exhibiting a hyper-accumulation (TF = 2.1) when treated with 11 mg F^- kg^{-1}, while for higher increasing concentrations (up to 220 mg F^- kg^{-1}) the TF ranged from 0.3 to 0.1.

Only one study assessed the impacts of AlF on the fluoride accumulation in rapeseed (25-75 mg F^- kg^{-1}) with TF ranging from 0.6 to 0.2 with a dose-dependent decreasing trend.

When fluoride was applied in the form of KF to soil (20-300 mg F^- kg^{-1}), the edible organs of triticale, narrow leaf-lupin, yellow lupin, sainfoin, radish and maize showed a TF always < 0.3.

As a well-known hyper-accumulator, the TF of the leaves of tea plants treaded with NH_4F or NaF (10-500 mg F^- kg^{-1}) reached markedly higher values compared to the TF of all the other considered species (up to 76). Only in one study the TF of tea was found to be lower than 1 (SF3 - Table 6).

In general, for almost all the crops, roots were the organs that accumulated fluoride most. An exception was represented by tea plant and Japanese camellia that, as expected, hyper-accumulated fluoride in the leaves which showed higher concentrations compared to roots and young shoots (Camarena-Rangel, et al., 2015, Ruan, et al., 2004, Yang, et al., 2016); this trend was moreover confirmed also in the previously mentioned field-scale studies (Fung, et al., 1999, Fung, et al., 2003, Ruan and Wong, 2001, Xie, et al., 2007). Another exception was represented by a study of Chen et al. (2017) on radish where the authors found that the accumulation of fluoride was highest in leaves than in roots. However, other studies conducted in radish confirmed the common higher concentration of fluoride in roots compared to leaves or, more generally, to aerial biomass (Chakrabarti and Patra, 2013a, Szostek and Ciećko, 2014). Furthermore, when mimicked sprinkler irrigation was applied (70-80% of water poured into the pot and 20-30% sprayed on plants) wheat (var. Raj. 3077) and barley (RD-2052) showed the highest concentration of fluoride in leaves, followed by stems, and then roots and grains (Agarwal and Chauhan, 2014, 2015). In other studies on cereals, roots were confirmed as the organs with the highest accumulation of fluoride, usually followed by the leaves and shoots and finally the grains (Chakrabarti, et al., 2013b, Jha, et al., 2013a, Mackowiak, et al., 2003, Szostek and Ciećko, 2014) or, in some other cases, as in the studies of Bhargava and Bhardwa (2011) on wheat (var. Raj. 4083) and Gautam and Bhardwaj (2010a) on barley (var. RD-2683), with the grains or crop ears accumulating more fluoride than shoot and leaves, respectively.

In crops as lady's finger and sugar cane, leaves were the second organ for fluoride concentration followed by fruits and shoots (lady's finger) or stem (sugar cane). At the opposite, in pakchoi, water spinach and lettuce, stems accumulated more fluoride than foliage (Zhang, et al., 2018). In mustard Ahmad et al. (2015) and Yadav et al. (2018) observed the following order: roots > seeds > shoots >

leaves, while Chakrabarti and Patra (2013a) found a higher concentration of fluoride in leaves than in seeds. In olive tree the pattern was: roots > shoot > leaves > fruits (Zouari, et al., 2014). In onion, after roots, the shoot accumulated more fluoride than the bulb and in slender amaranth leaves accumulated more than seeds (Jha, et al., 2009, Stanley, et al., 2002).

In many species (winter oilseed rape, narrow-leaf lupine, yellow lupine, phacelia and spinach) the accumulation pattern roots > aerial mass was observed but the partitioning among aerial organs was not investigated (Jha, et al., 2008b, Li, et al., 2018, Szostek and Ciećko, 2014). In some other cases, the accumulation pathway among organs was variable depending on the level of fluoride to which the plants were exposed (Bustingorri, et al., 2015, Bustingorri and Lavado, 2014, Das, et al., 2015).

3.3.2. Fluoride uptake

In the examined studies, an overall increasing trend of fluoride accumulation in organs of plants treated with rising concentrations of fluoride in soil or water was observed.

The highest fluoride concentration (3217 mg F^- kg^{-1} DM) was found in rice roots in case of a hydroponic experiment; this species showed a hyper-accumulation also in the shoot (395 mg F^- kg^{-1} DM) with respect to the level of fluoride to which the plants were subjected (30 mg F^- L^{-1}) (Mackowiak, et al., 2003). Tea leaves also showed a marked capacity to accumulate fluoride reaching up to 2553 mg F^- kg^{-1} DM in plants treated with 300 mg F^- kg^{-1} in soil (Yang, et al., 2016). Japanese camellia and sugar cane were also found to have high levels of fluoride in their tissues when treated with 30 mg F^- kg^{-1} of soil, up to 553 and 697 mg F^- kg^{-1} DM (Japanese camellia) and 521 and 120 mg F^- kg^{-1} DM (sugar cane) in roots and leaves, respectively. Considering its fast growth rate, sugar cane was best recommended by authors for phytoremediation purposes (Camarena-Rangel, et al., 2015). Very high concentrations were observed also by Zouari et al., (2014) in roots (up to 1070 mg kg^{-1} DM) and shoots (up to 570 mg F^- kg^{-1} DM) of olive tree treated with concentrations of fluoride in water up to 1900 mg F^- L^{-1}, and another extremely high value (1858 mg kg^{-1} DM) was observed by

Elrashidi et al. (1998) in the biomass of barley cultivated in acid soil and treated with 400 mg F^- kg^{-1}.

Concerning cereals, when plants were treated with low concentrations of fluoride the lowest value (0.9 mg F^- kg^{-1} DM) was observed in grains of wheat irrigated with 4 mg F^- L^{-1} while, among plants treated with the highest concentrations, the maximum value (54 mg F^- kg^{-1} DM) was found in grains of rice plants treated with water at 30 mg F^- L^{-1} (Bhargava and Bhardwaj, 2011, Chakrabarti, et al., 2013b).

Among the Brassicaceae, the lowest value (0.2 mg F^- kg^{-1} DM) was observed in cabbage treated with 10 mg F^- L^{-1} while the greatest (64 mg F^- kg^{-1} DM) was found in radish roots cultivated in soil with 300 mg F^- kg^{-1}. The maximum value for mustard seeds (22 mg F^- kg^{-1} DM) was found in the variety CS-14 irrigated with 75 mg F^- L^{-1}. Even they are not edible parts, it is worth noting that the shoots of winter oilseed rape and the leaves of radish reached 193 and 300 mg F^- kg^{-1} DM, respectively, when plants were grown in a soil contaminated with 1000 mg F^- kg^{-1} (Khandare and Rao, 2006, Li, et al., 2018, Szostek and Ciećko, 2014, Yadav, et al., 2018).

Regarding pulses, values in soybean ranged between 0.4 and 9.0 mg F^- kg^{-1} DM, and 2.4 and 28 mg F^- kg^{-1} DM in seeds and leaves, respectively. The concentration of fluoride in the aerial mass of narrow-leaf lupine, yellow lupine and sainfoin varied from 3 to 8, 4 to 33 and 3 to 28 mg F^- kg^{-1} DM when plants were cultivated in soils contaminated with fluoride contents from 0 to 60, 0 to 300 and 0 to 150 mg F^- kg^{-1}, respectively (Bustingorri, et al., 2015, Bustingorri and Lavado, 2014, Szostek and Ciećko, 2014).

Among the leaf-vegetables (elephant-head amaranth, slender amaranth, coriander, water spinach, lettuce and spinach) very high values were reached in spinach (up to 220 mg F^- kg^{-1} DM) treated with 800 mg F^- kg^{-1} in soil (Jha, et al., 2008b). In lettuce, water spinach, coriander and elephant-head amaranth, treated with waters from 0 to 10 mg F^- L^{-1}, the concentrations of fluoride ranged respectively between 2.0-2.8, 4.3-6.2, 4.0-16.4 and 4.0-50.0 mg F^- kg^{-1} DM (Chakrabarti and Patra, 2013a, Khandare and Rao, 2006). Quite high concentrations were observed also in other horticultural species such as for example in potato tubers (up to 21 mg F^- kg^{-1} DM), lady's finger fruits (up to 49 mg F^- kg^{-1} DM) and onion bulbs (up to 54 mg F^- kg^{-1} DM) when exposed to the highest levels of fluoride (220, 600 and 800 mg F^- kg^{-1} of soil respectively) (Das, et al., 2015, Jha, et al., 2009, Jha, et al., 2013b).

3.4. Effects of fluoride on plants

3.4.1. Effects on growth and biomass

A decrease in the total biomass of plants exposed to rising concentrations of fluoride was observed in many crops such as barley, rice, wheat, lady's finger, onion, soybean, pea, radish, spinach, triticale and olive tree (SF3 - Table 7). In contrast, Szostek and Ciećko (2017b) found that increasing levels of soil fluoride contamination (up to 300 mg F^- kg^{-1} of soil administered as KF) stimulated the biomass produced by radish, phacelia, narrow-leaf lupin, yellow lupin, winter oilseed rape and aerial parts of maize plants while the production of spring triticale straw and grains, maize roots, and aerial parts of lucerne was depressed (SF3 -Table 7).

Regarding yields, when soils were contaminated with NaF, dose-dependent decreases in yield of variable magnitude were observed in different crops. At maximum contamination doses of 300-450 mg F^- kg^{-1}, a reduction in yield of about 20 and 30% was observed in tea and soybean respectively. At concentration ranging from 800-1000 mg F^- kg^{-1}, yield were reduced by 20% in spinach and by 70-80% in onion and rapeseed. When fluorine was added to the soil in the form of KF triticale showed a dose-dependent decrease of up to 34% at maximum doses (200-300 mg F^- kg^{-1}) while a slight increase was observed in the roots of radish. Low NaF concentration (0.4-10 mg F^- L^{-1}) administered to lattuce and pak-choi via irrigation water led to a marked effect in terms of yield increases (up to 170 and 180%) that reached the peak at 3 mg F^- L^{-1} while in the same trial on water spinach, the yield was initially promoted and then suppressed. At higher concentrations (200-300 mg F^- L^{-1}) wheat and lady's finger were observed to exhibit a reduction in yield of approximately 50 and 60% respectively. In species as wheat, soybean, pea, mustard, radish, olive tree and lady’s finger some authors also observed a reduction in shoot and root length accompanied in some cases by a decrement in the number of leaves and leaf area, number of flowers, number and length of pods, number of seeds and 1000-grain weight (SF3 - Table 8).

Concerning tea plants, Yang, et al. (2016) observed that fluoride in hydroponic cultures, administered in the form of NaF, inhibited the growth of new roots and shoot tips, and coherently Pan, et al. (2020) found a reduction in root length by up to 50% in plants grown in hydroponic cultures at 16 mg F^- L^{-1}. In contrast, in a pot experiment Ruan, et al. (2003) observed that the growth of tea plants was not affected even at the highest level of fluoride contamination (100 mg F^- kg^{-1} of soil as NH_4F). Similarly, also Sharma et al. (2014) did not observe significant effects on shoot height, root length, leaf area, number of leaves, fresh leaf weight and dry leaf weight compared to control. No negative effects on the morphological parameters was also found by Camarena-Rangel et al. (2015) in a study assessing the phytoremediation efficiency in fluoride removal of Japanese camellia and sugar cane grown in hydroponic cultures with levels of fluoride up to 10 mg L^{-1}.

3.4.2. Visible symptoms

In species as onion, tip burning was observed (Jha, et al., 2009) while in wheat plants, chlorosis and necrosis symptoms were detected (Joshi and Bhardwaj, 2012). Leaf necrosis was found also by Yang et al. (2016) in tea plants treated with 300 mg F^- kg^{-1} of soil and visual symptoms of fluoride toxicity appeared as well in olive leaves in which necrosis was apical and/or marginal and progressively extended over the whole surface of the leaf lamina (Zouari, et al., 2014). On the other hand, Bustingorri et al. (2015) in soybean, Jha et al. (2013a, 2008b) in rice, wheat and spinach, and Ruan et al. (2003) in tea, despite a biomass reduction found in some cases, did not observe any visible injury.

3.4.3. Oxidative stress and defensive mechanisms

Superoxide dismutases (SODs) are prevalent metalloenzymes greatly involved in the immune response of living organisms. They are the first important defence enzymes within a plant cell being able to eliminate the oxidants in the cell parts affected (Ismail and Suroto, 2012), particularly toxic superoxide radicals (ROS). Biochemical changes observed in plants under fluoride stress may be related to the antioxidative defence mechanisms operating in the plant cells (Chakrabarti and Patra, 2015). The formation and accumulation of toxic oxygen species, like hydrogen peroxide (H_2O_2), lipid peroxidation (LP) and electrolyte leakage (EL) has been associated with various types of stresses (Cai, et al., 2016a). Other studies monitored the thiobarbituric acid reactive substances (TBARS) and malondialdehyde (MDA) production as markers of free radical formation in plant tissues. Moreover, under the influence of different environmental stresses, some authors reported a reduction in glutathione (GSH) (Śnioszek, et al., 2018), ascorbic acid (AA), total flavonoid (Flav) and total polyphenol content (Phe). Antioxidant enzymes like catalase (CAT), glutathione peroxidase (GPOX) and ascorbate peroxidase (APX) can catalyse the rupture of hydrogen peroxide H_2O_2.

Various authors observed an increase in SOD activity when plants were exposed to fluoride (SF3 - Table 9), but other studies showed that whereas lower fluoride concentrations stimulated the antioxidant system, higher fluoride levels caused a significant reduction of antioxidant enzyme activities with an increase of oxidative stress indicators such as H_2O_2, TBARS, LP and EL both in roots and leaves (Cai, et al., 2016a, Chakrabarti and Patra, 2015, Zouari, et al., 2017). In a study by Bustingorri et al. (2017) on soybean a significant decrease in GSH with respect to control was observed only at high fluoride concentration. Furthermore, Snioszek et al., (2018) found significant alterations in the level of AA, GSH, Flav and Phe in pea plants cultivated in contaminated soils, compared to the control plants.

Significant variations in the AA levels were also found in different vegetable species cultivated under field conditions in fluoride contaminated areas (Mondal and Gupta, 2015, Pal, et al., 2012).

3.4.4. Effects on the content of photosynthetic pigments

Total chlorophyll reduction is primarily caused by the chlorophyll collapse or inhibition of chlorophyll synthesis due to fluoride stress (Chang and Thompson, 1963). In most of the analysed studies, the chlorophyll content of fluoride-treated plants was found to decrease with respect to controls in a dose-dependent manner. In contrast, Stanley et al. (2002) found that in amaranth the chlorophyll a and b of leaf samples was not affected by fluoride. Together with the chlorophyll decline, several authors observed also a reduction in the content of carotenoids in species as lady's finger, mustard, rice and tomato (SF3 - Table 10).

Field-studies conducted on different plant species also reported a significant decrease in the chlorophyll content of most of the vegetables cultivated in the treated or fluoride-affected areas with respect to control plants (Mondal and Gupta, 2015, Pal, et al., 2012).

A reduction in photosynthetic and chlorophyll fluorescence parameters was also found by Cai et al. (2016a) in tea plants treated with fluoride doses higher than 5 mg L^{-1}. Joshi and Bhardwaj (2012) reported a modest effect of fluoride on chlorophyll b and a significant reduction in chlorophyll a in plants irrigated with increasing levels of fluoride. Furthermore, Camarena-Rangel, et al. (2015) found that the chlorophyll decrease in camellia species was manifested after 28 days for all the fluoride levels tested observing that this parameter was a better indicator of cellular integrity than others such as oxidation or wilting. Conversely, chlorophyll concentration in sugar cane plants grown in medium with 5 or 10 mg F^{-} L^{-1} was observed to increase with respect to control plants confirming the tolerance of this species to fluoride.

3.4.5. Effects on nutrients uptake

Zouari et al., (2017) suggested that the increased uptake of some minerals observed in olive could be interpreted as a defence response of plants to fluoride. Szostek and Ciećko (2015, 2017a) observed that the soil contamination with fluorine significantly affected the concentration of calcium, magnesium and phosphorus in all the tested species (S3 - Table 11). In contrast, tea plants subjected to fluoride treatments did not show any significant alteration in the concentrations of macro and microelements (K, Ca, Mg, S, P, Fe, Mn, Zn) in leaves (Ruan, et al., 2003, 2004) (S3 - Table 11).

3.4.6. Effects on free amino acids, proline, betaine and soluble sugars contents

A common response of plants to various types of environmental stresses is the overproduction and intracellular accumulation of free amino acids such as proline and betaine (Hayat, et al., 2012). In addition to other physiological functions, in fact, proline and betaine have an adaptive role in maintaining cell turgor or osmotic balance under stress conditions and are believed to have positive effects on enzyme and membrane integrity (Ashraf and Foolad, 2007, Dar, et al., 2016, Kavi Kishor, et al., 2015). Proline is a metal chelator, a signalling molecule and an antioxidant defence molecule preventing electrolyte leakage and normalizing concentrations of ROS (Dar, et al., 2016, Hayat, et al., 2012). Soluble sugars are also considered to have an important role in improving abiotic stress tolerance of plants by mediating osmotic adjustment and acting as ROS scavengers with antioxidant function. On the other hand, various kind of environmental stresses may compromise the photosynthesis efficiency and thus, reduce the soluble sugars supply (Keunen, et al., 2013, Ruan, et al., 2003, Sharma, et al., 2020).

Concerning proline or free amino acids accumulation in response to increasing fluoride doses, various authors consistently reported an increasing trend in species as lady’s finger, mustard, potato, olive, rice and tea (S3 - Table 12). In accordance with these findings also Pal, et al. (2012) in a field-scale experiment found that the level of proline of various plant species was higher in vegetables grown under fluoride stress conditions with respect to control plants. Conversely, Mondal and Gupta (2015) found a significant reduction in free amino acid contents in different species cultivated in a fluoride-polluted area in comparison to those grown in the control area. A mixed response was observed in the accumulation of betaine in tea leaves. At 5 mg F^- L^{-1} , in fact, betaine levels increased by up to 28% compared to control while at higher fluoride doses, betaine slightly decreased by up to 20% at 50 mg F^- L^{-1} (Cai, et al., 2016a).

As regards soluble sugars, a steady decreased with increasing fluoride concentration was observed in lady's finger and rice while their level increased in olive and potato tubers. In potato leaves an increase of soluble sugars content was observed in the range from 11-44 mg F^- kg^{-1} whereas a reduction of those compounds was found at 110 and 220 mg F^- kg^{-1} (Ahmed, et al., 2019b, Das, et al., 2015, Zouari, et al., 2016). In field experiments various vegetable species (with the exception of spinach and cabbage), showed a decrease in soluble sugars levels when cultivated in fluoride contaminated areas (Mondal and Gupta, 2015, Pal, et al., 2012).

3.4.7. Effects on protein, nitrogen, ash, fat and fibre contents

Studies that consider the effects of soil or water fluoride contamination on plant proteins or nitrogen contents are very few (Ahmed, et al., 2019b, Das, et al., 2015, Pan, et al., 2020, Saleem, et al., 2015, Szostek and Ciećko, 2017b) and, among these, just one investigated also the effects on ash, fat and fibre content (Saleem, et al., 2015). Protein or protein nitrogen content was found to significantly decrease with increasing fluoride doses in lady's finger, in the aerial mass of winter oilseed rape, and in potato tubers and leaves (SF3 - Table 13). Szostek and Ciećko (2017b) supposed that the fluoride-induced metabolic stress may alter the protein synthesis processes and accelerate their degradation and use for catabolic processes. A reverse relationship, *id est* an increase in the protein or N-protein content was observed in tomato, in the grains of spring triticale, in roots of black radish and in the aerial mass of Lucerne (SF3 - Table 13). At field scale, Mondal and Gupta (2015) observed an increase in the protein content of the plants grown in fluoride-treated plots, compared to control plots, in many vegetable species (onion, beet, celeriac, garlic, pea, wheat, rice and mustard while in spinach, cabbage, carrot, cucumber and lentil).

As regards the total nitrogen, its content increased with increasing soil fluoride levels in spring triticale, black radish, phacelia lucerne, maize aerial mass and roots of narrow-leaf and yellow lupine. Conversely, in the aerial mass of yellow lupine, the N-total content decreased (SF3 - Table 13).

Saleem, et al. (2015) observed that the ash content of two tomato varieties (Roma and Chinar) was not affected by increasing levels of soil fluoride contamination. In Chinar variety a significant reduction of fat content was found for soil fluoride concentrations above 50 mg F^- kg^{-1} while no significant effects were observed in the fibre content. At the opposite, in Roma variety, the fibre content was significantly reduced with all the treatments while the fat content was not affected (SF3 - Table 13).

3.4.8. Further effects

An interesting strategy to adapt and resist high concentrations of fluoride was observed by Cai, et al. (2016a) in leaves of tea plants consisting in the reduction in stomatal aperture with an increase in the epidermal hairs number. Similar results were found in young olive trees under fluoride stress, in which slight reductions of leaf relative water content (LRWC) and stomatal conductance were detected (Zouari, et al., 2016). Moreover, among the effects caused by fluoride on plants, serious damages to the ultrastructure of the cells were observed through transmission electron microscopy within a study in tea plant conducted by Li and Chen (2018).

4. Knowledge gaps and future research perspectives

At a global level, it is estimated that around 200 million people are at risk of hazardous exposure to fluoride, including about 66 million people in India and 45 million in China with a high prevalence also found in South America and Africa (Edmunds and Smedley, 2013).

The geographical distribution of the regions in which the fluoride in the water-soil-plant system has been investigated at field-scale so far, well reflects that of the high-fluoride groundwaters already reported by several authors (Ali, et al., 2016, Amini, et al., 2008, Edmunds and Smedley, 2013, Kimambo, et al., 2019). However, the analysis of the state of the art highlights that for some areas, such as for example the African Rift Valley, where groundwaters and surface waters recorded some of the highest concentrations of fluoride ever observed (Davies, 2008, Edmunds and Smedley, 2013), the contribution of the local food and feed contaminated crops to the daily fluoride human exposure is still poorly investigated.

Regarding India, rightly the areas in which the majority of the field-scale studies were conducted are recognised to be among the most affected of the country, first among all Rajasthan, where the risk of fluorosis concerns around 11 million people in 18 districts, and after that, Andhra Pradesh and Telangana which is the second-worst affected state in India (Ali, et al., 2016).

Concerning China, endemic fluorosis has been documented almost in all provinces and the main sources of exposure are considered to be high fluoride water, pollution from coal-burning and elevated consumption of brick tea (Kimambo, et al., 2019). This explains why a so high percentage of the studies conducted in this area (six out of twelve) focus on the accumulation of fluoride in tea plant.

The contribution of fluoride contaminated foods to the fluoride daily ingestion (and related HI) depends, as well as on the concentration of fluoride in the food itself, also on the amount of contaminated food ingested (USEPA, 1992). Therefore, to truly understand the potential impacts of the fluoride contamination of cropping systems on the health of the local communities, an essential aspect is to conduct nutritional surveys among the populations living in the contaminated areas.

From the literature analyses, it was found that, even though many field-scale studies have been conducted in the polluted regions, only a few authors carried out investigations about the eating habits of the rural populations. Further efforts in this direction would be necessary, not only to determine the EDI and HI associated with the consumed crops but also to identify which crops in a specific area give the greatest contribution to the fluoride daily ingestion (Rizzu, et al., 2020).

An effective adaptation strategy in contaminated areas could be represented by the choice of those species or cultivars that, with equal yields, show the least fluoride uptake capacity and accumulation in edible organs. With regard to this, although a certain range of plant species has been considered in the investigation on the fluoride absorption and accumulation additional research would be needed to strengthen the present knowledge on the already examined species and to include more food crops species in risk assessments. Furthermore, in order to compare the accumulation behaviour of different crop species, data on fluoride concentration in plant tissues, collected in field and pot scale experiment, should be always accompanied by the information related to the water-soluble fluoride (WS-F) in soil which allows to calculate the bio-concentration factor (BCF = concentration of F in plant tissue/concentration of WS-F in soil) (Bustingorri and Lavado, 2014). Compared to the TF, in fact, the BCF, based on the WS-F, which is the bioavailable soil fluoride fraction for plants, allows to compare the accumulation behaviour of different plant species regardless of the soil factors that could influence the mobility and the adsorption of fluoride in soils. At the opposite, these factors could interact with the species bio-accumulation attitude in determining the TF.

Concerning the effects of fluoride on plant health and production, since on most of the studied species just one or few experiments were conducted, we believe that further investigation would be necessary to confirm the existing knowledge. An aspect that would be also interesting to consider is related to the effect and the interaction linked to the presence of the counterion that accompanies the F^- in the pollutant (e.g. Na^+, K^+, NH_4^+, H^+, etc.) used in the trials conducted in controlled conditions. In this regard, could be convenient, for instance, setting up control treatments in which plants are exposed at the same concentration of the counterion without being exposed to the F^- (e.g. NaCl, KCl, etc.). Finally, greater attention should be reserved to the investigation on the effects of soil or water fluoride contamination on plant proteins or nitrogen contents, which represents an important factor influencing the nutritional quality of foods.

For clarity and data manageability purposes, in the present systematic review of literature, we decided to focus our attention only on those studies that consider the effects of soil and water fluoride contamination on the fluoride plant uptake and the productivity of adult plants at the physiological maturity stage. The choice of those boundaries led to the exclusion of a great number of papers concerning the effects of fluoride on plant germination and development in early stages. Given the importance of these parameters in determining plant yields in field-conditions, and the considerable amount of literature existing on this matter, we believe that this specific topic may also deserve a proper work of studies collection and analyses to be conducted with a systematic approach.

A further significant portion of literature that was excluded in our analysis regards all those studies in which the source of contamination is represented by the airborne fluoride. From the air, in fact, fluoride can be absorbed by the plant leaves via stomata leading to a progressive accumulation over time (Baunthiyal and Ranghar, 2015, Singh, et al., 2018). Since the two types of uptake mechanisms (by roots system or via stomata) may lead to different accumulation patterns and symptoms manifestation, we believe that studies focusing on one or the other route of entry must be reviewed and analysed separately. Airborne contamination of fluoride is a relevant issue particularly in the vicinity of industrial activities such as for example phosphate fertilizer manufacturing plants, brick kilns, aluminium and zinc smelters, glass and ceramic industries, etc. (Amundson, et al., 1990, Ben Abdallah, et al., 2006, Teixeira Rossi, et al., 2016) and the concentration of fluoride in the vegetation that grows in the nearby of these activities is utilized to bio-monitor the air contamination (Elloumi, et al., 2015). Due to the conspicuous literature produced on this matter and the significance of the subject dealt, a methodical overview of the existing knowledge on this topic would be really useful to orient future investigation on the base of the current findings.

Another topic, that has not been addressed in the present study which would worth to be considered for further studies, regards the effects of the interaction of fluoride with other water or soil elements (e.g. Ca, P, Al, etc.) and variables (e.g. pH, texture, water content, etc.) on the fluoride plant uptake and accumulation and its effect on crop productivity.

Finally, a really crucial aspect on which focus the attention in future investigation concerns the development and implementation of strategies aimed to mitigate the impacts of soil and water fluoride on plant, animal and human health. Researchers and stakeholders, in facts, would greatly benefit from a comprehensive framework of information aiming to collect all the existing options already identified to reduce the contribution of food crops to the human and animal fluoride dietary intake (e.g. use of water filters and soil amendments, phytoremediation, selection of species/variety with low bioaccumulation etc.). Such an overview would enable, in facts, the investigators to have a base on which identify and pursue the most promising research lines and the stakeholders to consider a set of possible effective mitigation options to test in their specific context.

5. Conclusive remarks

Through the systematic literature review process, a total of 87 studies were included in this work, among field-scale, pot, and hydroponic experimental studies, regarding the impacts of soil and water fluoride pollution on the safety and the productivity of food and feed crops at a global scale.

As regards the investigation on the effects of fluoride on plant health and production, even though some efforts in this direction were already made, in our opinion, additional research would be needed to strengthen the available evidence and confirm the current findings. Fluorine contamination led, in fact, to mixed results on crop yields that were suppressed or promoted, with more or less marked effects, depending on the contaminant (NaF or KF), the route of administration (directly via soil or via irrigation water), and the crop species under study. When soils were contaminated with NaF, dose-dependent yield decreases were observed in tea, soybean (up to 20-30% at 300-450 mg F^- kg^{-1}), spinach (up to 20-30% at 800 mg F^- kg^{-1}), onion and rapeseed (up to 70-80% at 800-1000 mg F^- kg^{-1}). The administration of NaF at low concentration (0.4-10 mg F^- L^{-1}) via irrigation water led to a marked effect in terms of yield increases (up to 170 and 180%) in lettuce and pak-choi (reaching the peak at 3 mg F^- L^{-1}) while, in the same trial, the yield of water spinach was initially promoted and then suppressed. At higher concentrations (200-300 mg F^- L^{-1}) wheat and lady's finger were observed to exhibit a reduction in yield of approximately 50% and 60% respectively. Adding fluorine to the soil in form of KF led to contrasting results: while triticale showed a dose-dependent decrease (up to 34% at 200-300 mg F^- kg^{-1}), yields of yellow lupine and rapeseed increases of up to 15% and 64% respectively (at 200-300 mg F^- kg^{-1}). Less marked increases were observed on the aerial biomass of radish and maize. At 60 mg F^- kg^{-1} narrow-leaf lupine showed a yield increase by 40%.

Many authors investigated also the toxic effects of fluoride on plants which was found to induce oxidative stress, reduction in chlorophyll content, alterations in the level of proline, betaine, soluble sugars, nitrogen and macro and micronutrients. In spite of that, the manifestation of symptoms such as visible injuries, decrease in root and shoot length was not always observed.

From the analysis of literature on controlled condition experiments, it came out that, with few exceptions (i.e. Japanese camellia and tea plant), plants tend to accumulate fluoride mostly in the root system. This could represent an issue mostly in the case of crops whose edible part is represented by the roots, such as radish which, for instance, was found to accumulate up to 296 mg F^- kg^{-1} DM in the Irkutsk region of Russia. Nevertheless, in most of the examined crops the accumulation of fluoride in other edible parts (e.g. leaves, fruits, tubers, bulbs, or seeds) was found to be dose-dependent, reaching considerable levels when plants were exposed to high fluoride doses. However, as far as the non-carcinogenic chronic effects of fluoride on human health are concerned, it is not possible to give *a priori* an absolute indication on the potential hazard related to the consumption of a contaminated food product. The contribution to the fluoride daily ingestion (and related HI), depends in fact, apart from the concentration of fluoride in the food itself, also on the amount of contaminated food ingested. In this regard, to better assess the potential impacts of the fluoride contamination of cropping systems on the health of the local communities, the investigation on the eating habits of the populations living in contaminated areas is fundamental. The areas where the populations mainly practice subsistence farming and the food products are self-consumed would be in fact the most affected. Among the examined field-scale experiments, the few authors that carried out nutritional surveys among local rural populations highlighted a significant contribution of the fluoride contaminated foods to the risk of overcoming the recommended dose enhancing the hazard of incurring fluorosis diseases.

In particular, in our opinion, field studies oriented to assess the extent of the fluoride contamination in the food chain would deserve greater investigation efforts in some seriously affected regions so far neglected. In fact, the majority of the field studies that were found through our analyses were located in Asia (India ~ 42% and China ~ 32%), while very few field experiments were found for Africa and South America despite in these regions the environmental fluoride contamination is serious and well documented.

Even though, as reported above, it is not possible to associate the levels of fluoride reached by crops with a predetermined level of risk, recommendation on the choice of the species to be grown in contaminated areas can however be based on the degree of fluoride mobility from the soil to the edible plant parts which is commonly measured through the BCF.

In contaminated areas, therefore, the cultivation of crops with the lowest BCFs in the edible parts is the most advisable. On the contrary, the planting of crops such as tea and sugar cane, which have found to be strongly fluoride hyper-accumulators (BCF> 1), should be likely avoided.

Funding

This research was funded by the EU H2020 FLOWERED project [690378] “de - FLuoridation technologies for imprOving quality of WatEr and agRo - animal products along the East African Rift Valley in the context of aDaptation to climate change” coordinated by Prof. Giorgio Ghiglieri, University of Cagliari.

References

Agarwal, R. and S. Chauhan. 2014. Bioaccumulation of sodium fluoride toxicity in Triticum aestivum var. Raj. 3077. International Journal of Food, Agriculture and Veterinary Sciences 4: 98-101.

Agarwal, R. and S. Chauhan. 2015. Bioaccumulation of sodium fluoride toxicity in plant parts at different phases and its impact on crop Hordeum vulgare (Barley) Variety RD 2052. International Journal of Multidisciplinary Research and Development 2: 16-21.

Ahmad, S., S. Ahmad, M. Ahmad, R. Shah and M. Nawaz. 2015. Bioaccumulation of fluoride ion at three flowering stages in different plant parts of mustard. Fluoride 48: 169-173.

Ahmed, S., M. Karamat, A. Haider, F. Jabeen, M.N. Ahmad, M. Ansari, et al. 2020. Ameliorative effects of salicylic acid on dry biomass and growth of Pisum sativum L. under sodium fluoride stress. Fluoride 53: 335-355.

Ahmed, S., K. Khalid, F. Jabeen, M. Ahmad, A. Zia, A. Haiderc, et al. 2019b. The effects of fluoride stress on Okra (Abelmoschus esculentus L.). Fluoride 52: 354-361.

Ahmed, S., K. Khalid, F. Jabeen, M. Ahmad, A. Zia, M. Muhajid, et al. 2019a. Productivity assessment of Okra under sodium fluoride stress. Fluoride 52: 348-353.

Ali, S., S. Thakur, A. Sarkar and S. Shekhar. 2016. Worldwide contamination of water by fluoride. Environmental Chemistry Letters 14: 291-315. doi:10.1007/s10311-016-0563-5.

Amini, M., K. Mueller, K. Abbaspour, T. Rosenberg, M. Afyuni, K. Møller, et al. 2008. Statistical modeling of global geogenic fluoride contamination in groundwaters. Environmental Science & Technology 42: 3662-3668. doi:10.1021/es071958y.

Amundson, R.G., A.J. Belsky and R.C. Dickie. 1990. Fluoride deposition via litterfall in a coastal-plain pine plantation in South Carolina. Water, Air, and Soil Pollution 50: 301-310. doi:10.1007/BF00280631.

Ashraf, M. and M. Foolad. 2007. Roles of glycine betaine and proline in improving plant abiotic stress resistance. Environmental and Experimental Botany 59: 206-216. doi:10.1016/j.envexpbot.2005.12.006.

Baunthiyal, M. and S. Ranghar. 2014. Physiological and biochemical responses of plants under fluoride stress: an overview. Fluoride 47: 287-293.

Baunthiyal, M. and S. Ranghar. 2015. Accumulation of fluoride by plants: potential for phytoremediation. Clean-Soil Air Water 43: 127-132. doi:10.1002/clen.201300353.

Begum, A., S. Harikrishna and I. Khan. 2008. Environmental fluoride level in Anekal Taluk of Bangalore District. Rasayan Journal on Chemistry 1: 774-781.

Ben Abdallah, F., N. Elloumi, I. Mezghani, J.P. Garrec and M. Boukhris. 2006. Industrial fluoride pollution of Jerbi grape leaves and the distribution of F, Ca, Mg, and P in them. Fluoride 39: 43-48.

Bharati, P., A. Kubakaddi, M. Rao and R.K. Naik. 2005. Clinical symptoms of dental and skeletal fluorosis in Gadag and Bagalkot districts of Karnataka. Journal of Human Ecology 18: 105-107. doi:10.1080/09709274.2005.11905816.

Bhargava, D. and N. Bhardwaj. 2011. Phytotoxicity of fluoride on a wheat variety (Triticum aestivum var. Raj. 4083) and its bioaccumulation at the reproductive phase. Asian Journal of Experimental Sciences 25: 37-40.

Bhattacharya, P., A.C. Samal, S. Banerjee, J. Pyne and S.C. Santra. 2017. Assessment of potential health risk of fluoride consumption through rice, pulses, and vegetables in addition to consumption of fluoride-contaminated drinking water of West Bengal, India. Environmental

Science and Pollution Research International 24: 20300-20314. doi:10.1007/s11356-017-9649-2.

Bilotta, G.S., A.M. Milner and I. Boyd. 2014. On the use of systematic reviews to inform environmental policies. Environmental Science & Policy 42: 67-77. doi:10.1016/j.envsci.2014.05.010.

Brahman, K.D., T.G. Kazi, J.A. Baig, H.I. Afridi, A. Khan, S.S. Arain, et al. 2014. Fluoride and arsenic exposure through water and grain crops in Nagarparkar, Pakistan. Chemosphere 100: 182-189. doi:10.1016/j.chemosphere.2013.11.035.

Bustingorri, C., K. Balestrasse and R.S. Lavado. 2015. Effects of high arsenic and fluoride soil concentrations on soybean plants. Phyton 84: 407-416.

Bustingorri, C. and R.S. Lavado. 2014. Soybean as affected by high concentrations of arsenic and fluoride in irrigation water in controlled conditions. Agricultural Water Management 144: 134-139. doi:10.1016/j.agwat.2014.06.004.

Bustingorri, C., G. Noriega, R.S. Lavado and K. Balestrasse. 2017. Protective effect exerted by soil phosphorus on soybean subjected to arsenic and fluoride. Redox Report 22: 353-360. doi:10.1080/13510002.2016.1276253.

Cai, H., Y. Dong, Y. Li, D. Li, C. Peng, Z. Zhang, et al. 2016a. Physiological and cellular responses to fluoride stress in tea (Camellia sinensis) leaves. Acta Physiologiae Plantarum 38: 144. doi:10.1007/s11738-016-2156-0.

Cai, H., X. Zhu, C. Peng, W. Xu, D. Li, Y. Wang, et al. 2016b. Critical factors determining fluoride concentration in tea leaves produced from Anhui province, China. Ecotoxicology and Environmental Safety 131: 14-21. doi:10.1016/j.ecoenv.2016.04.023.

Camarena-Rangel, N., Á.N. Rojas-Velázquez and M. del Socorro Santos-Díaz. 2015. Fluoride bioaccumulation by hydroponic cultures of camellia (Camellia japonica spp.) and sugar cane

(Saccharum officinarum spp.). Chemosphere 136: 56-62. doi:10.1016/j.chemosphere.2015.03.071.

Chakrabarti, S. and P.K. Patra. 2013a. Effect of fluoride on superoxide dismutase activity in four common crop plants. Fluoride 46: 59-62.

Chakrabarti, S. and P.K. Patra. 2015. Biochemical and antioxidant responses of paddy (Oryza sativa L.) to fluoride stress. Fluoride 48: 56-61.

Chakrabarti, S., P.K. Patra and B. Mondal. 2013b. Uptake of fluoride by two paddy (Oryza sativa L.) varieties treated with fluoride-contaminated water. Paddy and Water Environment 11: 619-623. doi:10.1007/s10333-012-0342-2.

Chen, Y., S. Wang, Z. Nan, J. Ma, F. Zang, Y. Li, et al. 2017. Effect of fluoride and cadmium stress on the uptake and translocation of fluoride and cadmium and other mineral nutrition elements in radish in single element or co-taminated sierozem. Environmental and Experimental Botany 134: 54-61. doi:10.1016/j.envexpbot.2016.11.002.

Choudhary, S., M. Rani, O.S. Devika, A. Patra, R.K. Singh and S.K. Prasad. 2019. Impact of fluoride on agriculture: A review on it’s sources, toxicity in plants and mitigation strategies. International Journal of Chemical Studies 7: 1675-1680.

CMH. 2012. National food safety standards. China, The ministry of health of the People's Republic of China. China Environmental Science Press: 1-17 (Chinese).

Collaboration for Environmental Evidence. 2013. Guidelines for systematic review and evidence synthesis in environmental management. Version 4.2. Environmental Evidence, Bangor, United Kingdom.

Cronin, S.J., V. Manoharan, M.J. Hedley and P. Loganathan. 2000. Fluoride: A review of its fate, bioavailability, and risks of fluorosis in grazed-pasture systems in New Zealand. New Zealand Journal of Agricultural Research 43: 295-321. doi:10.1080/00288233.2000.9513430.

Dagnaw, L.A., B.S. Chandravanshi and F. Zewge. 2017. Fluoride content of leafy vegetables, irrigation water, and farmland soil in the Rift Valley and in non-Rift Valley areas of Ethiopia. Fluoride 5: 409-429.

Dar, M., M. Naikoo, F. Rehman, F. Naushin and F. Khan. 2016. Proline accumulation in plants: roles in stress tolerance and plant development. In: I. N, N. R and A. K. N, editors, Osmolytes and plants acclimation to changing environment: emerging omics technologies. Springer, New Delhi. p. 155-166.

Das, C., U. Dey, D. Chakraborty, J.K. Datta and N.K. Mondal. 2015. Fluoride toxicity effects in potato plant (Solanum tuberosum L.) grown in contaminated soils. Octa Journal of Environmental Research 3: 136-143.

Davies, T. 2008. Environmental health impacts of East African Rift volcanism. Environmental Geochemistry and Health 30: 325-338. doi:10.1007/s10653-008-9168-7.

De Troiani, R.M., T.M. Sanchez and R.S. Lavado. 1987. Soil response and alfalfa fluoride content as affected by irrigation water. Fluoride 20: 14-17.

Ding, Z., Y. Li, Q. Sun and H. Zhang. 2018. Trace Elements in Soils and Selected Agricultural Plants in the Tongling Mining Area of China. International Journal of Environmental Research and Public Health 15: 202. doi:10.3390/ijerph15020202.

Edmunds, W.M. and P.L. Smedley. 2013. Fluoride in natural waters. In: O. S. e. al., editor Essentials of Medical Geology: Revised Edition. Springer, Netherlands. p. 311-336.

Elloumi, N., M. Zouari, L. Chaari, B. Ben Rouina, F. Ben Abdallah and M. Kallel. 2015. Morphological and physiological changes induced in Olea europaea and Prunus dulcis exposed to air fluoride pollution. Brazilian Journal of Botany 38: 99-106. doi:10.1007/s40415-014-0112-z.

Elrashidi, M.A., N. Persaud and V.C. Baligar. 1998. Effect of fluoride and phosphate on yield and mineral composition of barley grown on three soils. Communications in Soil Science and Plant Analysis 29: 269-283. doi:10.1080/00103629809369945.

Fung, K.F., Z.Q. Zhang, J.W.C. Wong and M.H. Wong. 1999. Fluoride contents in tea and soil from tea plantations and the release of fluoride into tea liquor during infusion. Environmental Pollution 104: 197-205. doi:10.1016/S0269-7491(98)00187-0.

Fung, K.F., Z.Q. Zhang, J.W.C. Wong and M.H. Wong. 2003. Aluminium and fluoride concentrations of three tea varieties growing at Lantau Island, Hong Kong. Environmental Geochemistry and Health 25: 219-232. doi:10.1023/A:1023233226620.

Gautam, R. and N. Bhardwaj. 2010a. Bioaccumulation of Fluoride in Different Plant Parts of Hordeum Vulgare (barley) Var. Rd-2683 from Irrigation Water. Fluoride 43: 57-60.

Gautam, R., N. Bhardwaj and Y. Saini. 2010b. Fluoride accumulation by vegetables and crops grown in nawa tehsil of Nagaur District (Rajasthan, India). Journal of Phytology 2: 80-85.

Gupta, S. and S. Banerjee. 2009. Fluoride accumulation in paddy (Oryza sativa) irrigated with fluoride-contaminated groundwater in an endemic area of the Birbhum district, West Bengal. Fluoride 42: 224-227.

Gupta, S. and S. Banerjee. 2011. Fluoride accumulation in crops and vegetables and dietary intake in a fluoride-endemic area of West Bengal. Fluoride 44: 153-157.

Hayat, S., Q. Hayat, M. Alyemeni, A. Wani, J. Pichtel and A. Ahmad. 2012. Role of proline under changing environments: a review. Plant Signal Behav 7: 1456-1466. doi:10.4161/psb.21949.

He, L., C. Tu, S. He, J. Long, Y. Sun, Y. Sun, et al. 2020. Fluorine enrichment of vegetables and soil around an abandoned aluminium plant and its risk to human health. Environmental Geochemistry and Health 1. doi:10.1007/s10653-020-00568-5.

He, X., P. Li, Y. Ji, Y. Wang, Z. Su and V. Elumalai. 2020. Groundwater Arsenic and Fluoride and Associated Arsenicosis and Fluorosis in China: Occurrence, Distribution and Management. Exposure and Health 12: 355-368. doi:10.1007/s12403-020-00347-8.

Ismail, M. and A. Suroto. 2012. Response of biochemical activities on selected rice plants towards ozone stress. International Conference on Nanotechnology and Chemical Engineering (ICNCS'2012). Bangkok, Thailand. p. 38-40.

Jezierska-Madziar, M. and P. Pinskwar. 2003. Fluoride in common reeds (Phragmites australis) sampled from the old Warta reservoirs near Lubon and Radzewice, Poland. Fluoride 36: 21-24.

Jha, S.K., T. Damodaran, C.L. Verma, V.K. Mishra, D.K. Sharma, V. Sah, et al. 2013a. Fluoride partitioning in rice (Oryza sativa) and wheat (Triticum aestivum) upon irrigation with fluoride-contaminated water and its risk assessment. South Asian Journal of Experimental Biology 3: 137-144.

Jha, S.K., A.K. Nayak and Y.K. Sharma. 2008b. Response of spinach (Spinacea oleracea) to the added fluoride in an alkaline soil. Food and Chemical Toxicology 46: 2968-2971. doi:10.1016/j.fct.2008.05.024.

Jha, S.K., A.K. Nayak and Y.K. Sharma. 2009. Fluoride toxicity effects in onion (Allium cepa L.) grown in contaminated soils. Chemosphere 76: 353-356. doi:10.1016/j.chemosphere.2009.03.044.

Jha, S.K., A.K. Nayak, Y.K. Sharma, V.K. Mishra and D.K. Sharma. 2008a. Fluoride accumulation in soil and vegetation in the vicinity of brick fields. Bulletin of Environmental Contamination and Toxicology 80: 369-373. doi:10.1007/s00128-008-9391-z.

Jha, S.K., Y.K. Sharma, T. Damodaran, V.K. Mishra and D.K. Sharma. 2013b. Bio-concentration of fluoride in Lady's finger (Abelmoschus esculentus) grown in contaminated alkaline soil and evaluation of exposure risk in human. Toxicological and Environmental Chemistry 95: 138-149. doi:10.1080/02772248.2012.745981.

Joshi, M. and N. Bhardwaj. 2012. Effect of fluoride on growth parameters and its accumulation in Triticum Aestivum var. Raj 3675. Fluoride 45: 297-301.

Kavi Kishor, P., P. Hima Kumari, M. Sunita and N. Sreenivasulu. 2015. Role of proline in cell wall synthesis and plant development and its implications in plant ontogeny. Frontiers in Plant Science 6: 544. doi:10.3389/fpls.2015.00544.

Kazi, T.G., H.I. Afridi, J.A. Baig and K.D. Brahman. 2019. Bioaccumulation of arsenic and fluoride in vegetables from growing media: health risk assessment among different age groups. Environmental Geochemistry and Health 41: 1223-1234. doi:10.1007/s10653-018-0207-8.

Keunen, E., D. Peshev, J. Vangronsveld, W. Van Den Ende and A. Cuypers. 2013. Plant sugars are crucial players in the oxidative challenge during abiotic stress: extending the traditional concept. Plant, Cell Environ. 36: 1242-1255. doi:10.1111/pce.12061.

Khandare, A.L. and G.S. Rao. 2006. Uptake of fluoride, aluminum and molybdenum by some vegetables from irrigation water. Journal of Human Ecology 19: 283-288. doi:10.1080/09709274.2006.11905892.

Kimambo, V., P. Bhattacharya, F. Mtalo, J. Mtamba and A. Ahmad. 2019. Fluoride occurrence in groundwater systems at global scale and status of defluoridation - State of the art. Groundwater for Sustainable Development 9: 100223. doi:j.gsd.2019.100223.

Lakshmi, D.V., K.J. Rao, T. Ramprakash and A.P.K. Reddy. 2016. Fluoride distribution in groundwater, soil and some crops grown in fluoride endemic area. Asian Journal of Environmental Science 11: 137-143.

Lakshmi, D.V., K.J. Rao, T. Ramprakash, A.P.K. Reddy and K.V. Kendra. 2017a. Bioaccumulation of fluoride in different plant parts of food crops grown in Narkatpally Mandal of Nalgonda District, Telangana. Environment & Ecology 35: 1753-1758.

Lakshmi, V.D., J.K. Rao, T. Ramprakash and A.P.K. Reddy. 2017b. Fluoride accumulation by crops grown in parts of Nalgonda District, Telangana State, India. Environment Conservation Journal 18: 79-86. doi:10.36953/ECJ.2017.181211.

Li, C. and Y. Chen. 2018. Effects of external calcium on the cell ultrastructure of tea plants under aluminium and fluoride stress. Fluoride 51: 243-251.

Li, Y., S. Wang, Z. Nan, F. Zang, H. Sun, Q. Zhang, et al. 2019. Accumulation, fractionation and health risk assessment of fluoride and heavy metals in soil-crop systems in northwest China. Science of the Total Environment 663: 307-314. doi:10.1016/j.scitotenv.2019.01.257.

Li, Y., S. Wang, D. Prete, S. Xue, Z. Nan, F. Zang, et al. 2017. Accumulation and interaction of fluoride and cadmium in the soil-wheat plant system from the wastewater irrigated soil of an oasis region in northwest China. Science of the Total Environment 595: 344-351. doi:10.1016/j.scitotenv.2017.03.288.

Li, Y., S. Wang, Q. Zhang, F. Zang, Z. Nan, H. Sun, et al. 2018. Accumulation, interaction and fractionation of fluoride and cadmium in sierozem and oilseed rape (Brassica napus L.) in northwest China. Plant Physiology and Biochemistry 127: 457-468. doi:10.1016/j.plaphy.2018.04.017.

Loganathan, P., M.J. Hedley, G.C. Wallace and A.H.C. Roberts. 2001. Fluoride accumulation in pasture forages and soils following long-term applications of phosphorus fertilisers. Environmental Pollution 115: 275-282. doi:10.1016/S0269-7491(01)00102-6.

Luo, J., D. Ni, C. He, S. Zhang, S. Liu, Y. Du, et al. 2019. Influence of exogenous calcium on the physiological, biochemical, phytochemical and ionic homeostasis of tea plants (Camellia sinensis (L.) O. Kuntze) subjected to fluorine stress. Plant Growth Regulation 87: 455-465. doi:10.1007/s10725-019-00478-2.

Mackowiak, C.L., P.R. Grossl and B.G. Bugbee. 2003. Biogeochemistry of fluoride in a plant-solution system. Journal of Environmental Quality 32: 2230-2237. doi:10.2134/jeq2003.2230.

Moeinian, K., M.R. Mehrasbi, H. Hassanzadazar, K. Kamali and E. Rabiei. 2016. Fluoride levels in soil and crops of tomato and onion farms of Zanjan. Journal of Human Environment and Health Promotion 2: 47-51. doi:10.29252/jhehp.2.1.47.

Moher, D., A. Liberati, J. Tetzlaff, D.G. Altman and T.P. Group. 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 6: e1000097. doi:10.1371/journal.pmed.1000097.

Mondal, D. and S. Gupta. 2015. Influence of fluoride contaminated irrigation water on biochemical constituents of different crops and vegetables with an implication to human risk through diet. Journal of Materials and Environmental Science 6: 3134-3142.

Nagaraju, A., A. Thejaswi and J. Aitkenhead-Peterson. 2017. Fluoride and heavy metal accumulation by vegetation in the fluoride affected area of Talupula, Anantapur district, Andhra Pradesh. Journal of the Geological Society of India 89: 27-32. doi:10.1007/s12594-017-0555-5.

Okibe, F., E. Ekanem, E. Paul, G. Shallangwa, P. Ekwumemgbo, M. Sallau, et al. 2010. Fluoride content of soil and vegetables from irrigation farms on the bank of river Galma, Zaria, Nigeria. Australian Journal of Basic and Applied Sciences 4: 779-784.

Ozsvath, D.L. 2009. Fluoride and environmental health: a review. Reviews in Environmental Science and Bio/Technology 8: 59-79. doi:10.1007/s11157-008-9136-9.

Pal, K.C., N.K. Mondal, R. Bhaumik, A. Banerjee and J.K. Datta. 2012. Incorporation of fluoride in vegetation and associated biochemical changes due to fluoride contamination in water and soil: a comparative field study. Annals of Environmental Science 6: 123-139.

Pan, J., D. Li, J. Zhu, Z. Shu, X. Ye, A. Xing, et al. 2020. Aluminum relieves fluoride stress through stimulation of organic acid production in Camellia sinensis. Physiology and Molecular Biology of Plants 26: 1127-1137. doi:10.1007/s12298-020-00813-2.

Pullin, A.S. and T.M. Knight. 2009. Doing more good than harm - building an evidencebase for conservation and environmental management. Biological Conservation 142: 931- 934. doi:10.1016/j.biocon.2009.01.010.

Pullin, A.S. and G.B. Stewart. 2006. Guidelines for systematic review in conservation and environmental management Conservation Biology 20: 1647-1656. doi:10.1111/j.1523-1739.2006.00485.x.

Ranjan, S. and S. Yasmin. 2015. Assessment of fluoride intake through food chain and mapping of endemic areas of Gaya District, Bihar, India. Bulletin of Environmental Contamination and Toxicology 94: 220-224. doi:10.1007/s00128-014-1396-1.

Rizzu, M., A. Tanda, L. Canu, K. Masawe, K. Mtei, M. Deroma, et al. 2020. Fluoride uptake and translocation in food crops grown in fluoride- rich soils. Journal of the Science of Food and Agriculture 100: 5498-5509. doi:10.1002/jsfa.10601.

Ruan, J., L. Ma, Y. Shi and W. Han. 2003. Uptake of fluoride by tea plant (Camellia sinensis L.) and the impact of aluminium. Journal of the Science of Food and Agriculture 83: 1342-1348. doi:10.1002/jsfa.1546.

Ruan, J., L. Ma, Y. Shi and W. Han. 2004. The impact of pH and calcium on the uptake of fluoride by tea plants (Camellia sinensis L.). Annals of Botany 93: 97-105. doi:10.1093/aob/mch010.

Ruan, J. and M.H. Wong. 2001. Accumulation of fluoride and aluminium related to different varieties of tea plant. Environmental Geochemistry and Health 23: 53-63. doi:10.1023/A:1011082608631.

Saini, P., S. Khan, M. Baunthiyal and V. Sharma. 2013. Mapping of fluoride endemic area and assessment of F-^{1} accumulation in soil and vegetation. Environmental Monitoring and Assessment 185: 2001-2008. doi:10.1007/s10661-012-2683-0.

Saleem, M., M.N. Ahmad, B.A. Khan, A. Zia, S.S. Ahmad, H.U. Shah, et al. 2015. Effects of soil fluoride on the growth and quality of two tomato varieties grown in Peshawar, Pakistan. Fluoride 48: 174-178.

Sharma, C., R.K. Gupta, R.K. Pathak and K.K. Choudhary. 2014. Impact of fluoride and VAM fungi on growth and foliar fluoride accumulation in tea plants. Fluoride 47: 15-22.

Sharma, P., P. Arora, D. Kapoor, K. Khanna, P. Atri, R. Bali, et al. 2020. The Role of Sugars in Improving Plant Abiotic Stress Tolerance. In: M. Khan, A. Singh and P. Poór, editors, Improving Abiotic Stress Tolerance in Plants. CRC Press, Boca Raton. p. 31-48.

Sharma, V., M. Yadav and N. Kumari. 2018. Aluminium Fluoride induced changes in chlorophyll a fluorescence, antioxidants and psb A gene expression of Brassica juncea cultivars. Journal of Plant Interactions 13: 472-482. doi:10.1080/17429145.2018.1522001.

Singh, G., B. Kumari, G. Sinam, Kriti, N. Kumar and S. Mallick. 2018. Fluoride distribution and contamination in the water, soil and plants continuum and its remedial technologies, an Indian perspective - a review. Environmental Pollution 239: 95-108. doi:10.1016/j.envpol.2018.04.002.

Singh, J., D. Singh and S.V.S. Chauhan. 2001. Effect of sodium fluoride on growth and yield in wheat (Triticum aestivum). Indian Journal of Agricultural Sciences 71: 41-43.

Singh, S., J. Singh and N. Singh. 2013. Studies on the impact of fluoride toxicity on growth parameters of Raphanus sativus L. Indian Journal of Scientific Research 4: 61-63.

Singh, V., M.K. Gupta, P. Rajwanshi, S. Mishra, S. Srivastava, R. Srivastava, et al. 1995. Plant uptake of fluoride in irrigation water by ladyfinger (Abelmorchus esculentus). Food and Chemical Toxicology 33: 399-402. doi:10.1016/0278-6915(95)00005-M.

Śnioszek, M., A. Telesiński, B. Smolik and H. Zakrzewska. 2018. Effect of Fluoride and Bentonite on Biochemical Aspects of Oxidative Stress in Pisum sativum L. Journal of Ecological Engineering 19: 164-171. doi:10.12911/22998993/82425.

Sokolova, L.G., S.Y. Zorina and E.N. Belousova. 2019. Zonal cultivars of field crops as a reserve for the phytoremediation of fluorides polluted soils. International Journal of Phytoremediation 21: 577-582. doi:10.1080/15226514.2018.1540545.

Stanley, V.A., A. Shaleesha, P.B.K. Murthy and K.S. Pillai. 2002. Retarding fluoride accumulation in Amaranthes viridis through liming and implications of phosphorous treatment. Journal of Environmental Biology 23: 265-269.

Subba Rao, N., B. Ravindra and J. Wu. 2020. Geochemical and health risk evaluation of fluoride rich groundwater in Sattenapalle Region, Guntur district, Andhra Pradesh, India. Human and Ecological Risk Assessment: An International Journal 26: 2316-2348. doi:10.1080/10807039.2020.1741338.

Szostek, R. and Z. Ciećko. 2014. Content of fluorine in biomass of crops depending on soil contamination by this element. Fluoride 47: 294-306.

Szostek, R. and Z. Ciećko. 2015. Effect of soil contamination with fluorine on the content of phosphorus in biomass of crops. Journal of Elementology 20: 731-742.

Szostek, R. and Z. Ciećko. 2017a. Effect of soil contamination with fluorine on the contents of calcium and magnesium in the biomass of crop plants. Fluoride 50: 41-58.

Szostek, R. and Z. Ciećko. 2017b. Effect of soil contamination with fluorine on the yield and content of nitrogen forms in the biomass of crops. Environmental Science and Pollution Research International 24: 8588-8601. doi:10.1007/s11356-017-8523-6.

Teixeira Rossi, Z.T., E.M. de Castro, G. Carvalho Pereira, J.P.R. Alves Delfino Barbosa, G.W. de Almeida Carvalho, M.A. de Lima Silva Rossi, et al. 2016. Ecophysiological, anatomical and ultrastructural characteristics of Vitex polygama Cham. (Verbenaceae) submitted to different concentrations of fluoride. Acta Scientiarum Biological Sciences 38: 481-489. doi:10.4025/actascibiolsci.v38i4.31400.

USEPA. 1992. Guidelines for exposure assessment. In: EPA, editor Federal Register Notice. Washington, DC. p. 22887-22938.

Vithanage, M. and P. Bhattacharya. 2015. Fluoride in the environment: sources, distribution and defluoridation. Environmental Chemistry Letters 13: 131-147. doi:10.1007/s10311-015-0496-4.

Wang, C., Z. Yang, L. Chen, X. Yuan, Q. Liao and J. Ji. 2012. The transfer of fluorine in the soil-wheat system and the principal source of fluorine in wheat under actual field conditions. Field Crops Research 137: 163-169. doi:10.1016/j.fcr.2012.08.001.

Wei, W., S. Pang and D. Sun. 2019. The pathogenesis of endemic fluorosis: Research progress in the last 5 years. J. Cell. Mol. Med. 23: 2333-2342. doi:10.1111/jcmm.14185.

WHO. 1999. World Health Organization. Guidelines for drinking-water quality. Vol 2. 2nd ed. World Health Organization, Geneva.

WHO. 2011. World Health Organization. Guidelines for drinking-water quality. 4th ed. World Health Organization, Geneva.

Wu, J. and Z. Sun. 2016. Evaluation of Shallow Groundwater Contamination and Associated Human Health Risk in an Alluvial Plain Impacted by Agricultural and Industrial Activities, Mid-west China. Exposure and Health 8: 311-329. doi:10.1007/s12403-015-0170-x.

Xie, Z., Z. Chen, W. Sun, X. Guo, B. Yin and J. Wang. 2007. Distribution of Aluminum and Fluoride in Tea Plant and Soil of Tea Garden in Central and Southwest China. Chinese Geographical Science 17: 376-382. doi:10.1007/s11769-007-0376-3.

Yadav, M., N. Kumari and V. Sharma. 2018. Phytoremediation efficiency of Brassica juncea cultivars at vegetative and reproductive growth stages under individual and combined treatment of fluoride and aluminium. International Journal of Phytoremediation 20: 922-929. doi:10.1080/15226514.2018.1448361.

Yadav, R.K., S. Sharma, M. Bansal, A. Singh, V. Panday and R. Maheshwari. 2012. Effects of fluoride accumulation on growth of vegetables and crops in Dausa district, Rajasthan, India. Advances in Bioresearch 3: 14-16.

Yadu, B., V. Chandrakar and S. Keshavkant. 2016. Responses of plants to fluoride: an overview of oxidative stress and defense mechanisms. Fluoride 49: 293-302.

Yang, Y., Y. Liu, C.-F. Huang, J. de Silva and F.-J. Zhao. 2016. Aluminium alleviates fluoride toxicity in tea (Camellia sinensis). Plant and Soil 402: 179-190. doi:10.1007/s11104-015-2787-8.

Yu, L., J. Zhang, C. Du, H. Yang and B.-C. Ye. 2018. Distribution and pollution evaluation of fluoride in a soil–water–plant system in Shihezi, Xinjiang, China. Human and Ecological Risk Assessment 24: 445-455. doi:10.1080/10807039.2017.1385386.

Zhang, J., L. Yu, H. Yang and B.-C. Ye. 2018. Migration and transformation of fluoride through fluoride-containing water for the irrigation of a soil–plant system. Human and Ecological Risk Assessment 25: 1048-1058. doi:10.1080/10807039.2018.1460577.

Zhao, S., Y. Liu, J. Ma, H. Mao, T. Lan, Y. Jiang, et al. 2015. Influence of fertilizers on fluoride accumulation in tea leaves and its remediation using polyphenol-Ce adsorbents. Rsc Advances 5: 6085-6091. doi:10.1039/C4RA10361K.

Zheng, D. and L. Sun. 2011. Fluorine contents in crops and water and its health risks assessment in Liaohe River Basin, China. 2011 International Symposium on Water Resource and Environmental Protection. IEEE. p. 2314-2316.

Zouari, M., C. Ben Ahmed, N. Elloumi, B. Ben Rouina, P. Labrousse and F. Ben Abdallah. 2016. Effects of Irrigation Water Fluoride on Relative Water Content, Photosynthetic Activity, and Proline Accumulation in Young Olive Trees (Olea europaea L. cv Chemlali) in Arid Zones. Fluoride 49: 366-372.

Zouari, M., C. Ben Ahmed, R. Fourati, D. Delmail, B. Ben Rouina, P. Labrousse, et al. 2014. Soil fluoride spiking effects on olive trees (Olea europaea L. cv. Chemlali). Ecotoxicology and Environmental Safety 108: 78-83. doi:10.1016/j.ecoenv.2014.06.022.

Zouari, M., N. Elloumi, K. Bellassoued, C. Ben Ahmed, M. Krayem, D. Delmail, et al. 2017. Enzymatic antioxidant responses and mineral status in roots and leaves of olive plants subjected to fluoride stress. South African Journal of Botany 111: 44-49. doi:10.1016/j.sajb.2017.03.039.

Figure legends

Supplemental Files

Supplemental File 1 (SF1) - Review Protocol

Supplemental File 2 (SF2) - List of publications included in the Systematic Review

Supplemental File 3 (SF3) - Over-sized Tables

Table 1 - Inclusion and exclusion criteria

Inclusion criteria	**Exclusion criteria**
Every kind of study assessing: ▪ the effects of soil and water fluoride on quali-quantitative characteristics of crop production ▪ fluorine uptake capacity of different kind of crops cultivated in soils and/or irrigated with water characterized by various levels of fluoride ▪ articles focusing only on adults plants ▪ microcosm, mesocosm and field-scale trials	First and second stages (screening title and abstract): ▪ Not on topic (misclassified) ▪ No relevant population (e.g. animals, humans, seedlings) ▪ No relevant exposure (e.g. airborne contamination) ▪ Methodological articles (e.g. procedures for determination of fluoride in soil or plant material) ▪ Full text not available ▪ Not in English Third stage (assessing full text): ▪ Same criteria of the first and second stages ▪ No relevant outcome ▪ Other reasons

Table 2 - Qualitative information extracted from the studies

Variable	**Description**
Country	Country where the study was conducted
Zone	Specific study area (village or town, city, district, province etc.)
Type of experiment	Pot/Field/Hydroponic (P/F/H)
Growing conditions	Greenhouse/Open field/Growth Chamber (G/O/GC)
Source of Exposure	Soil/Water (S/W)
Pollutant	Natural pollution, NaF, KF, NH_4F etc.
Other factors and levels	Other factors considered in the cases of factorial experiments and respective levels
Fertilization or amendment management	Type and doses of fertilizers/amendments applied
Species of plant	Scientific name of the studied plants
Variety	Varieties of the studied plants, if available
Phenology stage	Phenology stage at which plant where harvested
Accumulation pathway	Fluoride accumulation pathway among different plant organs
Effects of fluoride on plants	Visible injuries, oxidative stress, enzymatic activity etc.

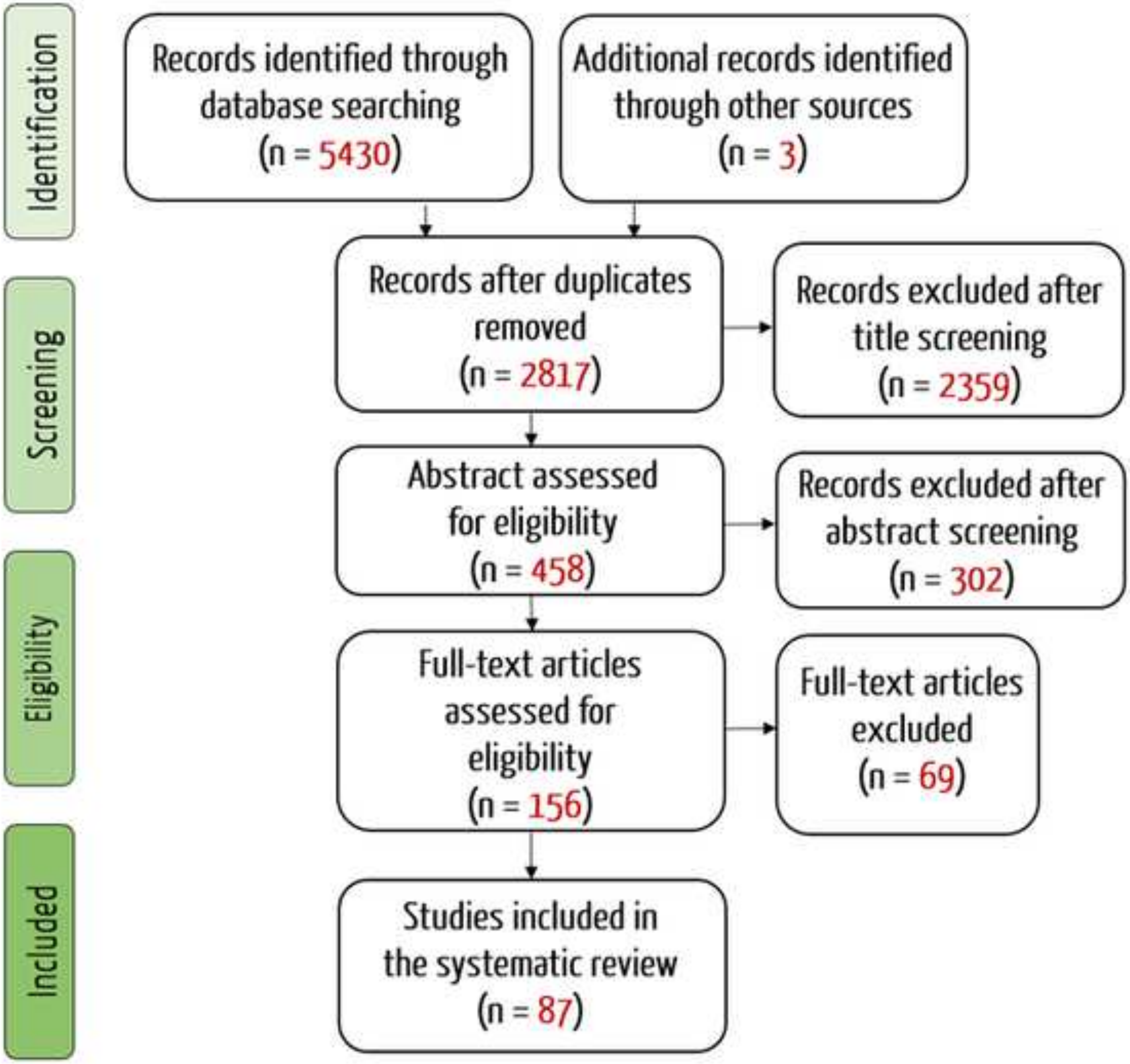
Table 3 - Quantitative information extracted from the studies

Kind of information extracted	Description
Sample size	Number of replicates per each treatment
Levels of fluoride exposure	Different levels of concentration of fluoride in water or soil
Levels of fluoride in different plant tissues	Different levels of concentration of fluoride in different plant parts (roots, stem, leaves, fruits, seeds etc.)
Yield of different plant parts	Dry matter of different plant parts or the entire plant biomass
Morphological traits	Morphological traits of the considered plant species (plant height, trunk diameter, leaf area, shoot length, root length, pod length, ear length, n. of leaves, n. of branches, n. of tillers, n. of ears, n. of flowers, n. of pods, n. of seeds, n. of seed pod^{-1}, n. of flowers ear^{-1}etc.)
Oxidative stress indicators	Oxidative stress indicators (H_2O_2: hydrogen peroxide, LP: lipid peroxidation, EL: electrolyte leakage, TBARS: thiobarbituric acid reactive substances, MDA: malondialdehyde, GSH: glutathione, AA: ascorbic acid, Flav: total flavonoid, Phe: total polyphenol content)
Antioxidant enzymes activity	Activity of the antioxidant enzymes (SOD: superoxide dismutase, CAT: catalase, GPOX: glutathione peroxidase and APX: ascorbate peroxidase)
Content of photosynthetic pigments	Content of photosynthetic pigments (chlorophyll a, chlorophyll b, carotenoids)
Nutrients uptake	Uptake rates of different nutrient elements (P, Ca, Mg, K, Al, S, Zn, Fe)
Content of free amino acids, proline, betaine and soluble sugars	Content of free amino acids, proline, betaine and soluble sugars
Content of protein, nitrogen, ash, fat and fibre	Content of protein, nitrogen forms (total nitrogen, protein nitrogen, nitrate nitrogen), ash, fat and fibre

Table 4 - Number of studies collected per each category of experiment type and kind of extractable data.

Type of experiments conducted in the included studies	N. of studies that reported data exclusively on F accumulation	N. of studies that reported data or results exclusively on the effects of F on plants	N. of studies that reported both kind of data
Field-scale	34	2	3
Pot	10	10	19
Hydroponic	0	2	4
Field + Pot	1	0	0
Field + Hydroponic	1	0	0
Pot + Hydroponic	0	0	1

Figure 1


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 5430)
Additional records identified through other sources (n = 3)
Records after duplicates removed (n = 2817)
Records excluded after title screening (n = 2359)
Abstract assessed for eligibility (n = 458)
Records excluded after abstract screening (n = 302)
Full-text articles assessed for eligibility (n = 156)
Full-text articles excluded (n = 69)
Studies included in the systematic review (n = 87)


3000 km
2000 mi

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.