Farida Bettiche, Warda Chaib, Ahmed Halfadji, Halima Mancer, Khalila Bengouga, Olivier Grünberger

Research Article

Microbial Biosystems 5(2) (2020) 2021.1031
10.21608/mb.2021.71824.1031

Contents lists available at Egyptian Knowledge Bank
Microbial Biosystems
Journal homepage: http://mb.journals.ekb.eg/

MICROBIAL BIOSYSTEMS
INTERNATIONAL SCIENTIFIC JOURNAL OF MICROBIAL BIOLOGY

The human health problems of authorized agricultural pesticides: The Algerian case

Farida Bettiche[1*], Warda Chaib[1], Ahmed Halfadji[2], Halima Mancer[1], Khalila Bengouga[1], Olivier Grunberger[3]

[1]*Scientific and Technical Research Center for Arid Regions, Campus Universitaire El Alia Nord, BP 1682-Biskra 07000, Algeria.*
[2]*Department of Sciences and Technology, Faculty of Applied Sciences, University Ibn-Khaldoun Tiaret, BP 78 P Zaâroura 14000, Tiaret, Algeria.*
[3]*IRD, UMR LISAH, 2 place Pierre Viala - 34060 Montpellier cedex 1 – France.*

INDEXED IN EMERGING SOURCES CITATION INDEX CLARIVATE ANALYTICS

ARTICLE INFO

Article history
Received 10 April 2021
Received revised 24 April 2021
Accepted 25 April 2021
Available online 28 April 2021

Corresponding Editor:
Dahshora K
Amrani S

Keywords
Pesticides
Hazards
WHO classification
PPDB
Human health

ABSTRACT

National authorized pesticides used in agriculture are one hot spot issue to human health especially for those working in the field. The aim of this study is to evaluate the health problems of authorized pesticides. Risk assessment was evaluated by 1) Toxicological classification of the WHO, and 2) Bio-Pesticides Database (BPDB) and Pesticide Properties Data Base (PPDB). The 2015 Algerian index of phytosanitary products used in agriculture includes 173 active ingredients (IAs) belonging to 83 chemical groups represented by 757 commercial formulations (CF) categorized into: 36% fungicides, 29% insecticides and 22% herbicides. One-third of the AIs are not approved according to EC 91/414 directive. Otherwise, only 3% and 6% of AIs are classified as extremely and highly hazardous respectively. About 47%, 37% and 30% of IAs can cause eye, skin and respiratory tract irritation respectively while approximately 32%, 13%, 10% and 8% of AIs can have/be reproductive and/or developmental effects, neurotoxic effects, cholinesterase inhibitors and endocrine disruptors respectively when only 5% and almost 3% of AIs are carcinogenic and mutagenic, respectively. It is essential to periodically update the list of authorized pesticides at national level in accordance with international legislation and bans. On the other hand, farmers must be aware of the health risks due to each AI to which they are exposed. Also, farmers must wear personal protective equipment (PPE). On the other hand, continuous epidemiological studies aimed primarily at farmers and their families must be carried out and the results of these studies must be accessible to researchers.

Published by Arab Society for Fungal Conservation

Introduction

The use of pesticides in agriculture is very excessive and around 85% of pesticide world production has been applied to chemical control of various pests (Kim al. 2017). Moreover, pesticides as a synthetic chemical compound

*** Corresponding author**
E-mail address: farida.bettiche@gmail.com (Farida Bettiche)

can be classified into many groups (herbicides, insecticides, fungicides, and so on) and based on the chemical composition of their active ingredients (AIs), they are more than thousands of pesticide formulations used in the environment that can affect the population health through different exposure routes (Blair et al. 2015). It is noteworthy that farmers constitute the population group directly exposed (occupational exposure) to high and repeated amounts of pesticides, much larger than the rest of the population as such, they are at greater risk than non-agricultural workers (Calvert et al. 2008). Indeed, farmers' exposure is due to preparation and application steps of pesticides and during the cleaning-up of equipment while consumers (including farmers) can be affected by pesticides due to consumption of food products containing high pesticide residues (Ojo 2016).

Many studies report that the greatest challenge is the lack of epidemiological data, with few studies on the impact of pesticides on human health (Jeyaratnam 1990, Bonner and Alavanja 2017, Benedetti et al. 2018). Despite this, it is generally agreed that predominantly chronic exposure to pesticides can adversely affect human health by causing acute and / or chronic effects/ diseases (Hamsan et al. 2017, Jacobsen-Pereira et al. 2018). Indeed, several studies carried out all over the world mainly concerning the effects of agricultural pesticides on farmers health can testify this like those of Lander et al. (2000), Stallones and Beseler (2002), Calvert et al. (2008), Mamane et al. (2015), Sonchieu et al. (2017), Buralli et al. (2018), Jacobsen-Pereira et al. (2018), Juntarawijit and Juntarawijit (2018), Patel and Sangeeta (2019). However, according to Blair et al. (2015), the determination of the dangerousness of pesticides to humans depends on the specific chemicals and health effects being considered. Indeed, not all pesticides have the same potency nor can they cause the same type or level of threat to human health (Gilden et al. 2010).

At the Algerian level, very few studies are reported dealing with the evaluation of the health risks due to pesticides and especially concerning those normally authorized. Citing the example of Slimani et al. (2011), who observed disturbances in reproductive biomarkers in male farmers working in greenhouses and exposed to pesticides. There is, however, an anti-poison control center which can provide data on acute poisonings and their causes.

We might believe that authorized pesticides are safe or less risky, but without extensive long-term studies and irrefutable evidence nothing is guaranteed. According to Gilden et al. (2010), even in a developed country like the United States, where all pesticides must be strictly registered with the United States Environmental Protection Agency (US EPA), the scientific report on the potential risk of pesticides to health due to the exposure is not required.

On 2015, globally, based on recent big databases "FAOSTAT (2020)", about 4.113.513 tons (t) of pesticides were used in agriculture and during the same year, China and the United States were the most consuming countries with1.772.421 and 407.779 t of this agrochemicals respectively (FAOSTAT 2020). According to the FAOSTAT data (http://www.fao.org/faostat/en / # data), during the same year, Algeria imported 17.566.404 t of pesticides of all types (for agricultural and non-agricultural uses) the equivalent of 108,603.74*103 US $ of which only 237 t (1.34%) were dangerous compounds while the quantity of pesticides imported for agricultural use was about 4517 t, of which 1740 t (39%), 323 t (7%) and 206 t (≈ 5%) were fungicides-bactericides, insecticides and herbicides, respectively. Bravo et al. (2011) had reported that import and export data of pesticides are a good indicator of usage trends and an informative source of assessing hazards but unfortunately, in Algeria's case, only the total imported quantities of pesticides listed by their biological activities were reported. Therefore, in the absence of data and national databases on the total quantities of imported active ingredients as well as the total use of pesticides per year, by type of agricultural production and by area, the assessment of all types of risk will be difficult at regional and national levels.

The main goal of this study is a first assessment of the human health risks of all synthetic biological pesticides for agricultural use authorized in Algeria (appearing in the 2015 index of phytosanitary products used in agriculture) through the Pesticide Properties DataBase (PPDB) and Bio-Pesticides Database(BPDB) in order to: i) Define actions at the legislative level, ii) Prioritization of lower risk active ingredients to use, iii) Raise users' awareness of their own health by adopting good phytosanitary practices (use of Personal Protective Equipment (PPE)).

Materials & Methods

The methodology is based on the use of three key elements: Firstly, according to the data published in the Algerian Index of phytosanitary products used in agriculture (2015 edition) (DPVCT 2015), we will identify the number of authorized pesticide commercial formulations (CFs) and the corresponding active ingredients (IAs). These pesticides are also classified into common groups according to their uses: insecticides, fungicides, acaricides, herbicides, mollucicides, nematicides and rodenticides.

However, only AIs of synthetic biological origins and the list of 18 pesticide AIs withdrawn from registration by the DPVCT at the end of 2013 are identified and classified. However, we have not categorized adjuvants, germination inhibitors, treatment of storage facilities, growth regulators and deficiency correctors which also appear in the index.

Secondly, AIs from first data analysis will be classified according to their hazardous potential for human health based on WHO international environmental guidelines (WHO 2010), as Extremely hazardous (Ia); Highly hazardous (Ib); Moderately hazardous (II); Slightly hazardous (III); Unlikely to present acute hazard in normal use (U); Not Listed/Obsolete as pesticide (NL/O) or Fumigant, not classified (FM).

Also, two databases: the pesticide properties database (PPDB)(https://sitem.herts.ac.uk/aeru/ppdb/en/index.htm) and the biopesticide database (BPDB)(https://sitem.herts.ac.uk/aeru/bpdb/index.htm) will be used to: i) classify these AIs according to the chemical groups to which they belong, ii) determine their regulatory status at European level according to Council Directive EC 91/414 of 15 July 1991 relating to the placing of plant protection products on the market, and iii) classify the AIs according to the specific human health issues they can cause : carcinogens, mutagens, endocrine disruptors, reproduction / development effect, cholinesterase inhibitors, neurotoxicants, respiratory tract irritants, skin irritants, skin sensitizers, eye irritants. It should be noted that only AIs marked with "Yes, known to cause a problem" by the used databases have been classified. Not taken into account in the classification the mentions: "Possibly, status not identified" or / and "No data found". Noting that, around 2016, the PPDB holds data for nearly 2300 pesticides active ingredients, which 300 parameters for each was stored, covering, among other things, human health risks assessment (Lewis et al. 2016).

Finally, we will take a concrete example of pesticides use by focusing on the most declared AIs by farmers practicing intensive agricultural system (market gardening under plastic greenhouses) or by sellers of phytosanitary products in the Biskra region where several studies on the use of pesticides followed by publications were carried out over a decade (between 2008 and 2018).

Results

In 2015, there were 200 active ingredients registered by Algerian data index to use in agricultural activities and 86.5% of them were synthetic organic compounds. Thus, these AIs were used in the preparation of 757 commercial formulations (CFs). Among the total registered CFs, there was 38% insecticides, 35% fungicides, 19% herbicides, 3% acaricides, 2% nematicides, 2% rodenticides and 1% molluscicides.

Classification of active ingredients of 2015 Algerian guide

According to their uses

By analyzing the 2015 index data, we found that: 36%, 29%, 22%, 5%, 4%, 3% and 1% of AIs are used as fungicides, insecticides, herbicides, acaricides, nematicides, rodenticides and molluscicides respectively. Also, it should be noted that insecticides take first place according to the importance of the number of CFs while fungicides hold the top of the list compared to the importance in number of active ingredients.

According to their chemical groups

The AIs belong to at least 83 chemical groups who have been identified. The best represented among them depending on the number of IAs and that of CFs are: Organophosphates (15AIs, 75 CFs), triazoles (13 AIs, 73 CFs), carbamates (13 AIs, 66 CFs), synthetic pyrethrinoids (12 AIs, 100 CFs) and neonocotinoids (4 AIs, 50 CFs) (Table 1). Organophosphates can act as insecticides (2/3 of AIs), as nematicides (4/15 of AIs) or as fungicide (1AI). While synthetic pyrethroids and neonicotinoids AIs are exclusively insecticides. Concerning carbamates AIs, 9/13, 3/13 and 1/13 of them, have fungicidal, insecticidal and Molluscicidal activity, respectively while all triazoles AIs act as fungicides.

Chlorpyrifos(-ethyl) is the best represented AI of the organophosphates because included into the formulation of more than 35 CFs (47% of total organophosphates CFs) while Tebunoconazole (17 CFs) and difenoconazole (12 CFs) are the most represented AIs of the triazoles (totaling together 40% of the CFs of this chemical group). Mancozeb is the most important AI of carbamates as it enters into the formulation of 34 CFs thus representing more than 51% of CFs in this group. The CFs containing deltamethrin (29 CFs), cypermethrin (25 CFs) and lambda cyhalothrin (23CFs) account for77% of the CFs of synthetic pyrethroids. For the group of neonicotinoids, two IAs: acetamiprid (19 CF) and imidacloprid (16 CF) are used in the manufacture of 70% of existing CFs. Concerning acaricides, propargite (sulfit ester) with 8 CFs is the best represented AI. Abamectin is also well represented and it's included in the formulation of 24 insecticides and 3 acaricides. The best represented herbicides AIs in relation to the number of CFs are glyphosate (phosphonoglycine), metribuzin (triazinone), 2.4 D (alkylchlorophenoxy) and Linuron (phenylurea) with 27, 22, 12 and 10 CFs respectively.

According to their regulatory status

Among the 18 pesticides which were used before and which were withdrawn from the approval list in December 2013 (Table 1), about 16 AIs (carbaryl, carbofuran, carbosulfan, fenthion, trichlorfon, methomyl, zineb,

Table 1 Pesticides-Active-ingredients included in the 2015 Algerian index of phytosanitary products, chemical groups and number of corresponding commercial formulations, WHO (2010) classification, approval status in European level and types of their health issues.

AIs(CF)	Chemical groups	WHO class	EU Status	Health issues	AIs(CF)	Chemical groups	WHO class	EU Status	Health issues
				Insecticides					
Spirotetramat(1)	Tetramic acid	III	A	4,9,10	Dimethoate(9)	Organophosphate	II	NA	5,10
Spirodiclofen (1)	Tetronic acid	NL	A	1	Fenthion*(2)		II	NA	5,7,8,10
Spiromesifen(1)		NL	A	9	Malathion*(0)		III	A	5,6
Chlorantraniliprole(4)	Anthranilamide	U	A	**	Methidathion(3)		Ib	NA	5,6,8
Diflubenzuron (4)	Benzoylurea	III	A	7	Parathion-methyl*(0)		Ia	NA	5,6
Lufenuron(6)		NL	NA	7,9	Phosalone*(0)		II	NA	5,6,7,8,10
Flufenoxuron(1)		III	NA	3,7	Phosmet(1)		II	A	4,5,6,10
Teflubenzuron(1)		U	NA	7	Pirimiphos-methyl (2)		II	A	5,7,8,10
Carbaryl*(0)	Carbamate	II	NA	3,4	Trichlorfon*(1)		II	NA	2,5,6,8
Carbofuran*(0)		Ib	NA	3,4	Indoxacarb (2)	Oxadiazine	III	A	6 ,9
Carbosulfan*(0)		II	NA	5,9	Fenpyroximate/ Fenpiroximate(1)	Pyrazolium	II	A	4,9
Fenoxycarb(2)		U	A	3,7,8,10	Acrinathrin(1)	Synthetic Pyrethroid	U	A	10
Methomyl* (0)		Ib	NA	5,7,10	Alpha- cypermethrin(8)		II	A	4,7,8
Oxamyl(3)		Ib	A	5,6	Beta-cyfluthrin(3)		Ib	A	4,6,7
Pirimicarb/Pyrimicarbe(4)		II	A	4,5,6,9,10	Beta-cypermethrin(3)		NL	NA	7,10
Abamectin(27of which 3 are A)	Micro-organism derived	Ib	A	4,6	Bifenthrin(4)		II	NA	3,6,9
Emamectin benzoate (3)		NL	A	10	Cypermethrin (25)		II	A	7,10
Bacillus thuringiensissubsp. Kurstaki/Btk(8)		III	A	9, 10	Deltamethrin (29)		II	A	3,6
Spinosad (2)		III	A	**	Fenpropathrin(1)		II	NA	7
Azadirachtin A(1)	Plant derived	NL	A	9	Fenvalerate*(0)		II	NA	3,7,8,10
Acetamiprid (19)	Neonicotinoid	II	A	8	Lambda – cyhalothrin (23)		II	A	7,9,10
Imidacloprid (16)		II	A	4	Tau - fluvalinate(1)		III	A	3,8
Thiacloprid (4)		II	NA	3,4,6,8,10	Tefluthrin (1)		Ib	A	6,8,10
Thiamethoxam (11)		NL	NA	**	Zeta-cypermethrin(1)		Ib	A	7
Buprofezin(1)	Unclassified	III	A	**	Pyridaben(1)	Pyridazinone	II	A	**
Pyriproxifen(1)		U	A	**	Pymetrozine(1)	Pyridine	NL	NA	1,4,7
Endosulfan* (0)	Organochlorine	II	NA	2,4,6	Metaflumizone(1)	Semicarbazone	NL	A	4
Acephate*(0)	Organophosphate	II	NA	3,5,6	Spinetoram(1)	Spinosym	U	A	4,9
Chlorpyrifos(-ethyl) (35)		II	NA	4,5,6	Cyromazine(2)	Triazine	III	NA	4,8
Chlorpyrifos- methyl(1)		III	NA	5,6,8,9					
Diazinon(5)		II	NA	5,6,7,8,10					
Dichlorvos(2)		Ib	NA	2,5,6,8,10					

Table 1 (continued).

AIs(CF)	Chemical groups	WHO class	EU Status	Health issues	AIs(CF)	Chemical groups	WHO class	EU Status	Health issues
				Fungicides					
Cyprodinil(2)	Anilinopyrimidine	III	A	7,8,9,10	Carboxin(1)	Oxathiin	III	A	9,10
Pyrimethanil(1)		III	A	**	Famoxadone(2)	Oxazole	U	A	**
Benalaxyl(1)	Acylamino acid	III	A	**	Hymexazol (6)		III	A	4,9,10
Fluopicolide (2)	Benzamide	NL	A	**	Fluazinam(1)	Phenylpyridinamine	NL	A	8,9,10
Zoxamide(1)		U	A	9,10	Fludioxonil(3)	Phenylpyrrole	U	A	8,10
Carbendazim(5)	Benzimidazole	U	NA	1,2,4	Captan(6)	Phthalimide	U	A	8,10
Thiabendazole(1)		III	A	**	Folpet/Folpel(3)		U	A	8,10
Thiophanate- methyl(5)		U	A	2,4,7,9	Metalaxyl(16)	Phenylamide	II	A	**
Iprovalicarb(2)	Carbamate	U	A	**	Metalaxyl –M(7)		NL	A	8,10
Mancozeb(34)		U	A	4,7,9, 10	Triforine(1)	Piperazine	U	NA	4,7,8
Maneb(5)		U	NA	4,7,8,9,10	Bupirimate(1)	Pyrimidinol	III	A	9,10
Metiram zinc(1)		U	A	8,9	Proquinazid(1)	Quinazolinone	NL	A	4
Propineb(9)		U	NA	**	Azoxystrobin(9)	Strobilurine	U	A	8,10
Propamocarb HCl (7)		U	A	8,9	Kresoxim-methyl(2)		NL	A	7,8,10
Thiram (4)		II	NA	8,9,	Pyraclostrobin(1)		NL	A	8,
Zineb*(1)		U	NA	4,7,8,10	Trifloxystrobin(2)		U	A	4
Ziram(2)		II	A	2,7,8,9,10	Ethaboxam(1)	Thiazole	NL	NA	**
Boscalid(1)	Carboxamide	U	A	**	Bitertanol(1)	Triazole	U	NA	3,4,9,10
Chlorothalonil (7)	Chloronitrile	U	NA	1,4,7,8,9,10	Cyproconazole(3)		II	A	7
Cymoxanil(9)	Cyanoacetamide oxime	II	A	4,9,10	Difenoconazole(12)		II	A	8,10
Iprodione(5)	Dicarboximide	III	NA	4,7	Epoxiconazole(1)		NL	A	1,4
Procymidone(5)		U	NA	1,3,4	Fluzilazole(1)		II	NA	4
Meptyldinocap(1)	Dinitrophenol	NL	A	8,10	Hexaconazole(7)		III	NA	8,9,10
Doguadine/Dodine(3)	Guanidine	II	A	8,10	Myclobutanil(4)		II	A	10
Fenhexamid(1)	Hydroxyanilide	U	A	**	Penconazole(7)		III	A	4
Fenamidone(2)	Imidazole	NL	NA	10	Propiconazole(9)		II	NA	7
Prochloraz(1)		II	A	4	Tebuconazole(17)		II	A	3,4,10
Mandipropamid(2)	Mandelamide	U	A	9	Tetraconazole(1)		II	A	**
Dimethomorphe(2)	Morpholine	U	A	7,8,10	Triadimenol(9)		II	NA	3,4,7,10
Spiroxamine(2)		II	A	7,8	Triticonazole(1)		III	A	**
Fosetyl- (aluminium) (6)	Organophosphate	U	A	7,10	Prothioconazole(2)	Triazolinthione	U	A	4
AIs(CF)	**Chemical groups**	**WHO class**	**EU Status**	**Health issues**	**AIs(CF)**	**Chemical groups**	**WHO class**	**EU Status**	**Health issues**
Acaricides									
Amitraz*(0)	Amidine	II	NA	6,8,9	Azocyclotin(1)	Organometal	II	NA	4,7,8,10
Bromopropylate(1)	Benzilate	U	NA	8,10	Cyhexatin(4)		II	NA	10
Hexythiazox(2)	Carboxamide	U	A	7,8,10	Fenbutatin-oxide(3)		III	NA	4,7,8,10
Bifenazate(1)	Hydrazine carboxylate	U	A	4,9	Tebufenpyrad(S) (1)	Pyrazolium	II	A	7,9
Dicofol*(0)	Organochlorine	II	NA	6,7,8,10	Propargite(8of which 1 is I)	Sulphite ester	III	NA	4,8,9,10

Table 1 (continued).

AIs(CF)	Chemical groups	WHO class	EU Status	Health issues	AIs(CF)	Chemical groups	WHO class	EU Status	Health issues
Herbicides									
Dicamba(3)	Benzoic acid	II	A	8,10	DNOC*(0)	Dinitrophenol	Ib	NA	2,6,8,9, 10
Glufosinate-ammonium(1)	Phosphinic acid	II	NA	4,6	Oxyfluorfen(10)	Diphenyl ether	U	A	1
2,4 D (2,4 PA) (12)	Alkylchlorophenoxy	II	A	4,6,7,10	Bromoxynil octanoate(1)	Hydroxybenzonitrile	II	A	3,9
Clodinafop- propargyl(4)	Aryloxyphenoxypropionate	NL	A	1,8,9,10	Bromoxynil*(0)		II	A	3,4,9
Diclofop- methyl(2)		II	A	7,9	Clomazone(1)	Isoxazolidinone	II	A	4
Fenoxaprop-P-ethyl(1)		O	A	7,8,9,10	Glyphosate(27)	Phosphonoglycine	III	A	8,10
Fluazifop- butyl(1)		O	NA	4,7,8,10	Chloridazon(1)	Pyridazinone	III	NA	8,10
Fluazifop-P-butyl(1)		III	A	9	Foramsulfuron(1)	Pyrimidinylsulfonylurée	NL	A	7
Haloxyfop-P-methyl/haloxyfop-R-methyl ester(1)		II	A	8,10	Pinoxaden(2)	Unclassified	NL	A	7,8,9,10
Propaquizafop(1)		U	A	9	Iodosulfuron(5)	Sulfonylurea	NL	A	6,7,8,10
Propyzamide(1)	Benzamide	U	A	1	Mesosulfuron(3)		NL	A	7,8,10
Bentazone(2)	Benzothiazinone	II	A	9,10	Sulfosulfuron(2)		NL	A	10
Paraquat *(1)	Bipyridylium	II	NA	2,7,8,10	Tribenuron- methyl(4)		U	A	7,9
Aminopyralid acid(1)	Pyridine compound	U	A	10	Prosulfocarb(1)	Thiocarbamate	II	A	7, 8,9,10
Trichlopyracid(3)		II	A	4,9,10	Prometryn(1)	Triazine	III	NA	3
Clethodim(1)	Cyclohexanedione	NL	A	8	Metribuzin(22)	Triazinone	II	A	4
Cycloxydim(1)		III	A	4,8,10	Propoxycarbazone - sodium(2)	Triazolone	NL	A	**
Pendimethalin(2)	Dinitroaniline	II	A	4,7,8,9,10	Florasulam(2)	Triazolopyrimidine	U	A	7
Trifluralin(5)		U	NA	3,4,7,9	Pyroxsulam(1)		NL	A	8,9,10
Cloquintocet-mexyl(5)	Unclassified	NL	NA	8,9,10	Linuron(10)	phenylurea	III	NA	4,8,10
Molluscicides (M), Nematicides (N)and Rodenticides (R)									
Metaldehyde (M) (6)	Cyclo-octane	II	A	10	Fosthiazate (N) (1)	Organophosphate	NL	A	5, 10
Methiocarb (M) (1)	Carbamate	Ib	NA	5, 6	Cadusafos (N) (1)		Ib	NA	5
Dazomet (N) (2)	Dithiocarbamate	II	A	8,9,10	Difenacoum (R) (7)	Hydroxycoumarin	Ia	NA	4
1,3-dichloropropene (N) (2)	Halogenated hydrocarbon	FM	NA	4,7,8,9,10	Brodifacoum (R) (2)	Hydrocoumarin	Ia	NA	**
1,2-dichloropropane (N) (1)	Organochlorine	O	NA	3,4,7,8,9,10	Chlorophacinone (R) (1)	Indandione anticoagulant	Ia	NA	4
Ethoprophos (N) (3)	Organophosphate	Ia	NA	5,9	Bromadiolone (R) (1)	Coumarin anticoagulant	Ia	A	4
Fenamiphos/Phenamiphos (N) (3)		Ib	A	4,5,6,10	Bromethalin (R) (1)	Unclassified	Ia	NA	6,8,10

Notes :AIs :Active Ingredients ; CF: Commercial Formulations;(*) :AIs withdrawn from homologation in Algeria on December 2013; (**) : No specific human health issues, or no data has been found regarding this active ingredient according to PPDB and BPDB;1.Carcinogen, 2. Mutagen, 3. Endocrine disrupter, 4. Reproduction / development effects, 5. Acetyl cholinesterase inhibitor, 6. Neurotoxicant, 7. Respiratory tract irritant,8.Skin irritant, 9. Skin sensitiser,10. Eye irritant;.A : Approved; NA : Not Approved, Ia = Extremely hazardous; Ib = Highly hazardous;II = Moderately hazardous;III = slightly hazardous;U = Unlikely to present acute hazard in normal use;FM = Fumigant, not classified; NL/O =not listed/ Obsolete as pesticide, not classified endosulfan, acephate, parathion-methyl, phosalone, fenvalerate, amitraz, dicofol, DNOC and paraquat s/f dichloride) are not approved in the European level according to EC 91/414 Directive as well as at national level. However, 4 IAs reappear in the Algerian index of 2015, two of them are organophosphates (fenthion and trichlorfon), one is a carbamate (zineb) and one is bipyridylium (paraquat s/f dichloride). In the other hand, while malathion and bromoxynil are still approved at European level they are not any longer at Algerian one according to the 2015 index.

In summary, on the basis of the Algerian data index of 2015 where 173 IAs are identified and therefore approved at national level as indicated in table 1, more than 56 of the IAs are not approved by the EC 91/414 Directive. These unapproved IAs are represented by 2/3 of organophosphates IAs, 1/2 of pyrethroid IAs and 1/4 of neonicotinoid IAs as well as 38% of the total IAs of each of the triazole and carbamate groups (Table 1).

According to their toxicity

We can indicate that from 173 AIs identified in the data Algerian index we have found only one nematicide (ethoprophos) and five rodenticides that have been classified as extremely hazardous (la) to human health. Also, 10 AIs Among the list are classified as highly hazardous (Ib) including 4 organophosphates (dichlorvos, methidathion, fenamiphos and cadusafos), 3 pyrethroids (beta-cyfluthrin, tefluthrin and zeta-cypermethrin), 2 carbamates (oxamyl and methiocarb) and 1 AI derived from microorganism (abamectin) (Table 1). These 2 classes (Ia) and (Ib) group only 3% and 6% of all AIs respectively. Also, about 30% of AIs are classified as having moderate hazard (II), 24 % as potential or acute hazard (U), 17 % are slightly hazardous (III) and 17 % are not listed by WHO 2010 list while Obsolete pesticides and fumigants represent only 3% of AIs (Figure 1).

According to diseases and health disorders caused

First of all, we note that several AIs can cause several health problems at the same time. According to the databases, we can indicate that 47% and 37% of the 173 IAs can cause eye and skin irritation respectively while the respiratory tract irritation (inhalation exposure) and skin sensitizers are caused by 30 % of AIs each. Still according to the data analysis of the databases, we found that 32 % of AIs can cause reproductive and/or development problem effects in humans. Also, IAs which can be neurotoxic, cholinesterase inhibitors and endocrine disruptors hold 13, 10 and 8% respectively. However, only 5% and almost 3% of AIs are carcinogenic and mutagenic, respectively. Moreover, 82% of cholinesterase inhibitors AIs belonging to organophosphates group (mostly insecticides and nematicides) and carbamates (insecticides and molluscicides). In the light of the analyzed data in the present case, we found that no AI with fungicide, herbicide or acaricide activity act as cholinesterase inhibitor. In addition, none of the fungicides are neurotoxic while 72% of insecticides can cause this effect. Among the 22 AIs which are neurotoxic, 36%, 18% and 14% belong to organophosphates, synthetic pyrethroids and carbamates, respectively. A large proportion of AIs that have effects on reproduction and development are fungicides (38%), insecticides (25%) and herbicides (18%) (Figure 2). Moreover, triazoles, carbamates and organophosphates are the most representing groups of AIs which can cause those effects.

Discussion

Concrete case: market gardening in greenhouses in Biskra

The predominance of use of fungicides, insecticides, acaricides or herbicides specialties depends among other things on the type of cropping system and its intensive state.Regarding the use of pesticides on market gardening greenhouses in Biskra (Algeria), where several studies have been conducted, insecticides-acaricides-fungicides use constitutes ≥ 99% (according to surveys among farmers) in Belhadi et al. (2016), Bettiche (2017), Rahmoune et al. (2018) studies (Table 2).According to these authors, there is no herbicidal use. However, herbicides were mentioned by sellers of plant protection products inRamdaniet al. (2009) and Soudani et al. (2020) studies.

According to their chemical groups and active ingredients

In Biskra region, according to farmers' declarations in Belhadi et al. (2016) study, the following chemical groups (in order of importance): synthetic pyrethroids, triazoles, organophosphates, neonicotinoids, avermectins, benzimidazoles, carbamates, organochlorines and dithiocarbamates hold more than 2/3 (almost 69%) of the uses in greenhouses. The majority of these chemical classes appear as important in Bettiche et al. (2019), Rahmoune et al. (2018) and Soudani et al. (2020) studies with the exception of organochlorines which is absent in Soudani et al. (2020) study. This result is consistent with the declarations of the sellers of phytosanitary products in Bettiche et al. (2017) study where the chemical groups to which belong the most sold AIs are carbamates, organophosphates, triazoles (5 AIs each), neonicotinoids, synthetic pyrethroids (4 AIs each), avermectins, benzimidazoles, dicarboximides, organochlorines and phenylamides (2 Als each). Roldán-Tapia et al. (2005) report that in southeastern Spain, growers in intensive greenhouse agriculture are exposed to pesticides, mainly organophosphates and carbamates. In Burkina Faso, Son et

Table 2 Farmer's self-declaration of short-term health effects due to their exposure to pesticides and percentage of non-use of personal protective equipment under intensive system in Biskra region.

Authors	**Ramdani et al. (2009)**		**Belhadi et al. (2016)**	**Bettiche (2017)**	**Rahmoun et al. (2018)**	**Soudani et al. (2020)**
Localities	**Sidi Okba**	**Tolga**	**Sidi Okba, Ain Naga, M'Ziraa**	**Sidi Okba, Ain Naga, M'Ziraa El Ghrous, Doucen, Lioua**	**M'Ziraa El Ghrous,**	**Ain Naga Doucen**
Short-term health effects				**%**		
Respiratory/ coughing/Chest pain	12	4	NR	NR	2.50	28
Dermatological (skin irritation)	14	2	NR	NR	5	16
Ocular (Teary eyes/eye irritation)	19	29	NR	NR	11.25	9
Gastrointestinal /Nausea/Stomach-ache	2	6	NR	NR	12.50	3
Headache/ Dizziness	27	39	NR	NR	53.75	6
Tiredness/Weakness	23	19	NR	NR	6.25	NR
Muscle cramps /Lumbar pain	3	1	NR	NR	3.75	NR
% of No use of PPE	59	73	77	37	89	>50

Notes:PPE:Personal Protective Equipment; NR: Not Reported

Table 3 The most declared active ingredients according to farmers and/or sellers of phytosanitary products in the Biskra region, their environmental risk score and their carcinogenic potential.

Authors	Bettiche et al. (2017)		Bettiche (2017)	Rahmoun et al. (2018)	Soudani et al. (2020)	Soudani et al. (2020)	Classification of AIs according to their carcinogenic potential	
Type of surveyed samples	Sellers		Farmers	Farmers	Farmers	Farmers + Sellers		
Most declared AIs	Rank/ ZE[1] and ZW[2]		%	%	%	ERS[3]	USEPA[4] (2017)	IARC[5] (2020)
Acetamiprid	6	5	52	10	40	2.33	NLTBCH	NL
Imidacloprid	7	6	21	5	20	5.30	Grp E	NL
Endosulfan	4	1	25	4	0	ND	NLTBCH	NL
Dicofol	1	1	10	4	0	ND	Grp C	Grp 3
Cypermethrin	8	7	17	4	35	3.13	Grp C	NL
Lambda-cyhalothrine	10	11	17	1	8	ND	Grp D	NL
Chlorpyrifos(-ethyl)	14	12	21	ND	5	ND	Grp E	NL
Diazinon	12	17	10	0	20	5.00	NLTBCH	Grp 2A
Triadimenol	4	4	21	6	19	6.13	Grp C	NL
Hexaconazole	9	9	11	2.5	19	5.50	Grp C	NL
Mancozeb	8	8	21	4	31	1.40	Grp B	NL
Maneb	16	15	11	1	15	ND	Grp B	Grp 3
Methomyl	9	4	5	0	0	ND	Grp E	NL
Carbendazim	1	1	8	1	1	ND	Grp C	NL
Thiophanate-methyl	2	2	17	1	4	ND	LTBCH	NL
Abamectin	3	3	92	12.5	79	4.00	NL	NL
Emamectin benzoate	2	3	24	1	19	ND	Grp E	NL

Notes: ND: No Data; NL: Not Listed;1: ZibanEast sellers;2:Ziban West sellers;3:Environmental Risk Score; 4: United States Environmental Protection Agency; 5: International Agency for Research on Cancer: https://monographs.iarc.fr/list-of-classifications/ consulted on 04/10/2020; Grp: Group;Group 2A: Probably carcinogenic to humans, Group 2B:Possibly carcinogenic to humans; Group 3: Not classifiable as to its carcinogenicity to humans, Group B: Probable Human Carcinogen.Group C: Possible Human Carcinogen., Group D: Not Classifiable as To Human Carcinogenicity., Group E: Evidence ofNon-Carcinogenicity for Humans;LTBCH: Likely to Be Carcinogenic to Humans;NLTBCH: Not Likely to Be Carcinogenic to Humans.

al. (2017) found that, pyrethroids, organophosphate compounds and neonicotinoids are the most widely used chemical groups used by tomato growers.

Health effects

Since, the pests are eukaryotes, like human beings, the targets of pesticides occur in human body too (Patel and Sangeeta 2019). The effects of pesticides can be immediate, acute to chronic due to chronic and prolonged exposure at low doses which can be expressed by various diseases.

Short term effects/Acute effects

Pesticide uptake occurs mainly through the skin and eyes, by inhalation, or by ingestion (Jeyaratnam 1990). It seems logical then, that the immediate effects of pesticides on health follow the routes of entry. Indeed, we have seen (Table 1) that a large proportion of AIs cause eye, skin and respiratory irritation. On the other hand, Bradberry et al. (2005) reported that when pyrethroids are used in confined spaces their absorption through the skin and inhalation increases. According to Table 2, headache / dizziness, ocular problems, tiredness / weakness, respiratory, dermatological and gastrointestinal problems, muscle

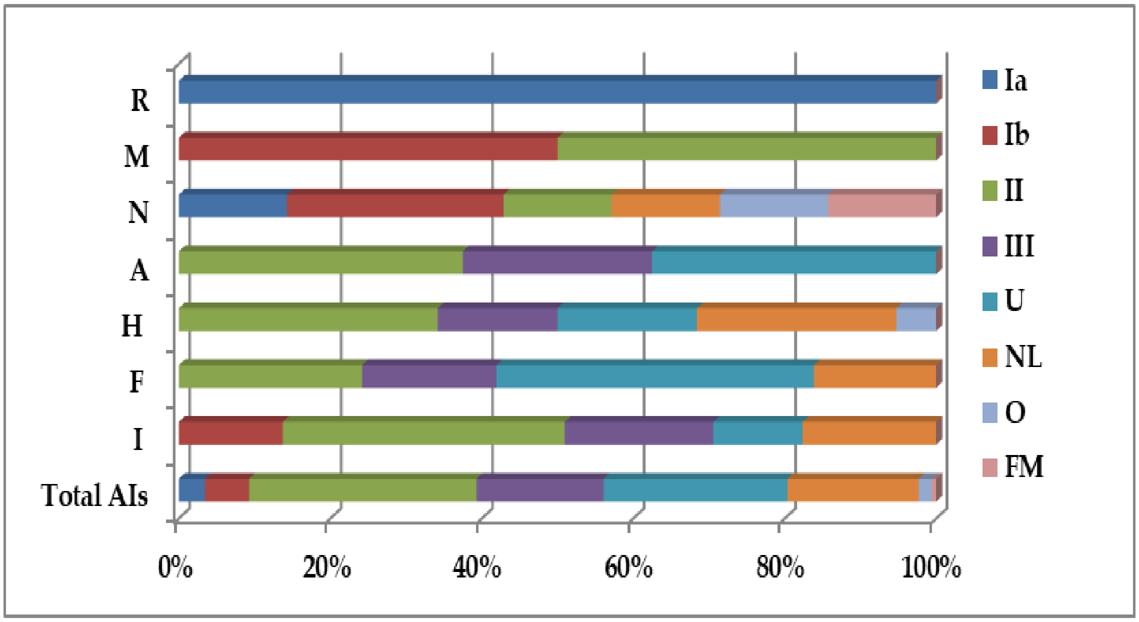

Fig 1. Distribution of organic active ingredients (from the 2015 Algerian index of phytosanitary products) according to toxicity classes established by WHO (2010).

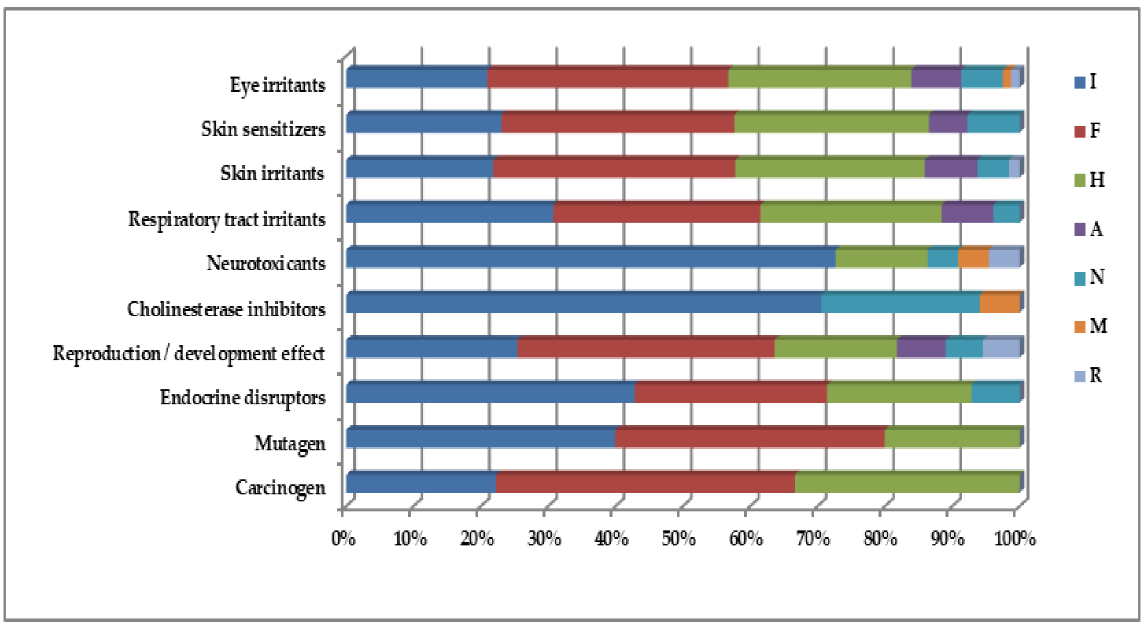

Fig 2. Health issues resulting from the active ingredients according to the PPDB and the BPDB databases.

cramps / lumbar pain are the most reported effects by farmers in market gardening under greenhouse in Biskra. In Gaza Strip, Yassin et al. (2002) reported that about prevalence of self-reported toxicity symptoms among farmers working in open or closed fields, burning sensation in eyes/face was the commonest symptom (64.3%). In Burkina Faso in Son et al. (2017) study, the surveyed farmers experienced skin irritation (26%), hot flashes (19%), nose flow and cough (15%), eye conditions (8%) and headaches (4%). In Nigeria, Ugwu et al. (2015) reported that majority of the farmers (74%) suffered from at least one health symptom associated with pesticide handling mainly skin irritation, followed by dizziness, Headaches, difficult breathing and tightness in the chest and blurred vision. In Philippines, the farmers and farm workers (n=68) in Del Prado-Lu (2015) study reported experiencing itchiness of the skin (63.8 %), redness of the eyes (29.3 %), muscle pains (27.6 %), and headaches (27.6 %), as being related to their pesticide exposure.

Rehman et al. (2014) reported that mainly Type II pyrethroids cause paresthesia, which is characterized by transient burning/tingling/itching sensation of the exposed skin. Also, pyrethroid ingestion gives rise within minutes to a sore throat, nausea, vomiting abdominal pain, dizziness, headache and fatigue (Bradberry et al. 2005). Which is consistent with the health disorders caused by a large proportion of AIs (Table 1 & Figure 2) and with described symptoms by the surveyed farmers. On the other hand, organophosphate pesticides (OPs) are widely used and readily absorbed through the skin (Cocker et al. 2002). In addition of being irritants, OPs are cholinesterase inhibitors and neurotoxicants (Ross et al. 2013, Sánchez-Santed et al. 2016). Moreover, according to Slotkin (2004), the organophosphates have additional effects on brain development that may overshadow their cholinergic component. In addition, Priyadharshini et al. (2017) found in their study that chronic exposure to organophosphate pesticides do affect the cardio respiratory system among farmers. About neonicotinoids, environmental exposure may lead to typical cardiovascular and nervous symptoms (Taira 2014). Moreover, Ohayo-Mitoko et al. (2000) results suggest the presence of a relation between exposure to pesticides (mainly organophosphates and carbamates) and acetylcholinesterase inhibition, acetylcholinesterase activity, and respiratory, eye, and central nervous system symptoms. Also, symptoms found to occur following exposure to AChE inhibitors such as OP and carbamate pesticides include fatigue, joint and muscle symptoms, sleep effects, headaches, skin effects, cognitive effects, mood effects, and neurological effects (Gupta et al. 2011).

Personal Protective Equipment (PPE)

Thus, to prevent pesticides from entering the body and affect their health, farmers must protect themselves by using appropriate personal protective equipment (PPE) (Yarpuz-Bozdogan 2018). Indeed, according to Remor et al. (2009), the use of PPE seems to be important in the prevention of contamination. Moreover, the results of Hatzilazarou et al. (2004) study underline the need for protective measures that operators must take when spraying pesticides in the closed environment of a greenhouse. In Algeria (Biskra), for example concerning market gardening under greenhouse, over 50%, 77% and 89% of farmers have never used PPE according to the survey results of Soudani et al. (2020), Ramdani et al. (2009), and Rahmoune et al. (2018) respectively (Table 2). Similar findings about none or low frequency usage of protective measures amongst farmers have been reported in several studies conducted in Tunisia (Jeder et al. 2018), Morocco (Berni et al. 2016), Nigeria (Ugwu et al. 2015), Burkina Faso (Son et al. 2017), Ethiopia (Mengistie et al. 2017), Tanzania (Mwabulambo et al. 2018), Iran (Sharifzadeh et al. 2017), Greece (Damalas and Abdollahzadeh 2016, Rezaei et al. 2018) and Brazil (Buralli et al. 2018). In our opinion, there are several possibilities linked to the lack of wearing of PPE: Farmers may not find pesticides to be very toxic to their health (Palis et al. 2006), or they may not believe of PPEs usefulness (Sharifzadeh et al. 2017). Either, despite the fact that they would wear the PPE, these latter are not available or are available but do not meet their requirements (expensive, hot and uncomfortable) (Okonya and Kroschel 2015, Mengistie et al. 2017, Buralli et al. 2018). So, understanding factors affecting the use of PPE during handling of pesticides is of major importance for the design of adapted interventions to minimize exposure among farmers (Damalas and Abdollahzadeh 2016). Also, encouraging the proper use of PPE could greatly reduce poisoning cases and cost of illness (Macharia 2015). Effectively, several studies demonstrate the effectiveness of wearing the PPE to reduce considerably pesticide-related acute symptoms and decrease risk of neurological symptoms (Macharia 2015, Nurcandra et al. 2018).

Long term effects/Chronic diseases: Cancer

Regarding the risk of cancer of the most declared AIs representing the most important chemical groups (Table 3), we find that: Acetamiprid and imidacloprid (neonicotinoids) are unlikely to be carcinogenic to humans and show non-carcinogenicity to humans (Group E) respectively. Regarding synthetic pyrethroids, it is possible that cypermethrin causes cancer in humans (group C) according to the USEPA classification (2017) (US EPA Office of Pesticide Programs 2017). While lambda cyhalothrin is not classifiable as to human carcinogenicity. For diazinon and chlorpyrifos (organophosphates). Diazinon is probably carcinogenic to humans (Group 2A) according to the International Agency for Research on Cancer(IARC, 2020) classification while there is evidence of non-carcinogenicity to humans for chlorpyrifos (Group E) (US EPA Office of Pesticide Programs 2017).Triadimenol and hexaconazol (triazoles) are both possible human carcinogens (group C).Mancozeb and maneb (carbamates) are probable human carcinogens (group B) (USEPA, 2017).Of benzimidazoles, carbendazim is a possible human carcinogen (group C) while thiophanate-methyl is likely to be carcinogenic to humans. For abamectin and emamectin benzoate (Micro-organism derived), while the first AI is not classified, there is evidence of non-carcinogenicity for humans regarding emamectinbenzoate. However, in their studies Ghenabzia et al. (2014) in the region of South East Algeria (Oued Souf) concluded that abamectin has mutagenic potential. Moreover, some pesticides based on some of these AIs are produced nationally by ALPHYT (Algerian phytosanitary company) including: cypermethrine, lambda cyhalothrin, chlorpyriphos ethyl and abamectin (Bettiche 2017).Interestingly, abamectin ranked third in sales according to Biskra region suppliers (Bettiche et al.2017) and had the highest percentage of use according to farmer's declarations in all cited studies (Table 3).This is probably due to the large number of its existing commercial formulations (27CFs) as well as the fact that abamectin is used as an insecticide and acaricide. On the other hand, dietary exposure includes exposure through contaminated food or water it generally involves consumption of treated agricultural produce (FAO/WHO 2016). Indeed, Belguet et al. (2019) have found after the assessing of health risk associated with vegetables growing under greenhouse conditions in Setif (Eastern of Algeria) that contamination by abamectin suggest higher possibility of potential health risk. It turns out that triadimenol, hexaconazol, imidacloprid, diazinon, abamectin and cypermethrin obtained also the highest Environmental Risk Score (ERS) in Soudani et al. (2020). To endorse some of these results, Bettiche (2017) had found residues of hexaconazol and imidacloprid detected in agricultural soils in 2 localities belonging to the Biskra region, respectively Sidi Okba and El Ghrous.

We have noticed that after more than 3 years of their withdrawal from the Algerian approval (since December 2013) and from the Algerian index of phytosanitary products for agricultural use (2015 version), the following IAs are no longer declared by farmers: endosulfan and dicofol (organochlorines) and methomyl (carbamates). This period would correspond to the period of inventory disposal. However, dicofol was reintroduced as an acaricide (with 2 commercial formulations) in the latest (2017) version of the Algerian phytosanitary index (MADR 2018). Ghenabzia and Lanez (2014) also reported that dicofol is one of the 10 most used pesticides by farmers in El Oued region, a city bordering Biskra (South East Algeria). They concluded in their work that dicofol had mutagenic and / or carcinogenic potential.

Conclusions

The list of priority active substances is not exhaustive, it will be wise to conduct research based on the quantification of products (active substances) sold in order to have a classification of AIs to be prioritized.

Studies on the chemical groups and active materials considered to be dangerous to human health (by priority) must be carried out because, even after being banned from use, withdrawn from approval, they sometimes continue to be used illegally and they continue to persist in environmental compartments for very long periods. It is logical to say that some chronic diseases are due to past use of currently banned AIs.

Despite the approval status of AIs in the 2015 Algerian guide, a significant number of them remains detrimental to human health, especially for direct users / applicators who are farmers in rural areas. The latter must be made conscious of the risks of each of these AIs and make them aware of the precautions they must take starting by wearing PPE. Also, studies should be conducted to understand reasons that influence the non-use of these PPE in order to resolve them.

About the legislative side, it is primordial to continually update the list of phytosanitary products authorized at the national level in relation to those at the international level, as well as in relation to recent results of epidemiological research concerning these substances and to initiate such research at national level in order to establish the cause-and-effect relationships that can link occupational diseases in agriculture to the use of these AIs. Also, for each published index, a toxicity-risk guide should be attached; this guide should also contain instructions for good phytosanitary practices in several languages and with illustrations.

It should also be noted that the symptoms or diseases were self-declared by the farmers, the latter must carry out periodic medical checks or it would be preferable to involve specialized doctors in this type of research to validate the questionnaires (health side) and / or to examine subjects and carry extensive tests if necessary.

Otherwise, aware of the difficulty of banning the total use of pesticides for multiple reasons which the main one being linked to the threat to food security. It is nevertheless possible to resort to new nanotechnology as the next revolutionary technology in agriculture which can provide sustainable tools to minimize, focus and control the nanopesticides inputs (Chhipa 2017a) increasing, thus, their efficacy and durability (Kah et al. 2013, Kookana et al. 2014, Kah 2015) and reducing their negative impacts on environment (solving eutrophication and residual pesticide accumulation problem), on nontarget organisms and humans (Chhipa 2017b, Gahukar and Das 2020). Also, more research should focus on biopesticides as an alternative to conventional pesticides and it would be better if we could combine the two solutions as nanobiopesticides.

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgements

The authors thank The General Directorate of Scientific Research and Technological Development (DGRSDT) for its support.

Funding

No funding was used to conduct this research.

References

Belguet A, DahamnaS, AbdessemedA, OuffroukhK, GuendouzA(2019) Determination of abamectin pesticide residues in green pepper and courgettegrowing under greenhouse conditions (Eastern of Algeria –Setif–). Eurasia J Biosci 13(2) : 1741–1745.

Belhadi A, Mehenni M, Reguieg L, Yakhlef H (2016) Pratiques phytosanitaires des serristes maraichers de trois localités de l'est des Ziban et leur impact potentiel sur la santéhumaine et l'environnement. Revue Agriculture 1: 9–16.

Benedetti D, Lopes Alderete B, Telles de Souza C, Ferraz Dias J, Niekraszewicz L, Cappetta M, Martínez-López W, Da Silva J (2018) DNA damage and epigenetic alteration in soybean farmers exposed to complex mixture of pesticides. Mutagenesis 33(1): 87–95.

Berni I, Atassi M, Nejjari C, Zidouh A, El Jaafari S, El Rhazi K (2016) Pesticide use pattern among farmers in a rural district of Meknes: Morocco. OALib 03(12): 1–19.

Bettiche F,Grünberger O, Chaïb W, Mancer H, Bengouga K, Belhamra M (2019) Origins of pesticide residues in agricultural soils in Biskra (South-East Algeria): survey vs . detection. JARA 13(2): 12–29.

Bettiche F (2017) Usages des produits phytosanitaires dans les cultures sous serres des Ziban (Algérie) et évaluation des conséquences environnementales possibles.PhD thesis, Mohamed KhiderUniversity, Biskra.

Bettiche F, Grunberger O, Belhamra M (2017) Contamination des eaux par les pesticides sous système de production intensive (serres), cas de Biskra, Algérie. Courrier du savoir23(Juin) : 39–48.

Bio-Pesticides Database (BPDB). https://sitem.herts.ac.uk/aeru/bpdb/index.htm.

Blair A, Ritz B, Wesseling C, Freeman LB (2015) Pesticides and human health. OEM 72(2): 81–82.

Bonner MR, Alavanja MCR (2017) Pesticides, human health, and food security. Food Energy Secur. 6(3): 89–93.

Bradberry SM, Cage SA, Proudfoot AT, Allister Vale J (2005) Poisoning due to pyrethroids. Toxicol. Rev. 24(2): 93–106.

Bravo V, Rodríguez T, Van Wendel De JoodeB, Canto N, Calderón GR, Turcios M, Menéndez LA, Mejía W, Tatis A, Abrego FZ, De La Cruz E, Wesseling C (2011) Monitoring pesticide use and associated health hazards in Central America.Int J Occup Environ Health 17(3): 258–69.

Buralli R J, Ribeiro H, Mauad T, Amato-Lourenço LF, Salge JM, Diaz-Quijano FA, Leão RS, Marques RC, Silva DS, Guimarães JRD (2018) Respiratory condition of family farmers exposed to pesticides in the state of Rio de Janeiro, Brazil. Int. J. Environ. Res. Public Health, 15(6), 1203.

Calvert GM, Karnik, J, Mehler L, Beckman J, Morrissey B, Sievert J, Barrett R, Lackovic M, Mabee L, Schwartz A, Mitchell Y, Moraga-McHaley S (2008) Acute pesticide poisoning among agricultural workers in the United States, 1998–2005. Am. J. Ind. Med., 51(12), 883-898.

Chhipa H (2017) a Nanofertilizers and nanopesticides for agriculture. Environ. Chem. Lett, 15(1): 15-22.

Chhipa H (2017) b Nanopesticide: current status and future possibilities. Agric Res Technol, 5(1): 1-4.

Cocker J, Mason HJ, Garfitt SJ, Jones K (2002) Biological monitoring of exposure to organophosphate pesticides.Toxicol. Lett. 134(1–3): 97–103.

Damalas CA, Abdollahzadeh G (2016) Farmers' use of personal protective equipment during handling of plant protection products: determinants of implementation. Sci Total Environ. 571 : 730–736.

DPVCT (2015) Index des produits phytosanitaires à usage agricole, Juillet 2015. Direction de la protection des végétaux et des contrôles techniques.http://www.inpv.edu.dz/institut/wpcontent/uploads/2016/03/INDEX_PRODUITS_PHYTO_2015.pdf.

Food and Agriculture Organization of the United Nations (FAO) (2020) http://www.fao.org/faostat/en/#data/RP.

FAO/WHO (2016) International code of conduct on pesticide management, guidelines on highly hazardous pesticides. http://www.fao.org/3/i5566e/i5566e.pdf.

Gahukar RT, Das RK (2020) Plant-derived nanopesticides for agricultural pest control: challenges and prospects. Nanotechnol. environ. eng. 5(1) : 1-9.

Ghenabzia I, Lanez T (2014) Évaluation de risque mutagène et cancérogènes des quelques pesticides utilisés par les agriculteurs dans la région du sud Algérien." In Premier séminairenational Sur l'electrochimie-Méthodes et Applications43–47.

Ghenabzia I, Lanez T, Didi OuldElhadj M, Ahmedi R (2014) Use of electrochemical technics as a tool for the evaluation of the in vitro mutagenic potential of abamectin pesticide. JOCPR 6(12): 274–279.

Gilden RC, Huffling K, Sattler B (2010) Pesticides and health risks. JOGNN 39(1): 103–110.

Gupta RC (Ed.) (2011) Toxicology of organophosphate and carbamate compounds. Academic Press.

Hamsan H, Ho YB, Zaidon SZ, Hashim Z, Saari N, Karami A (2017) Occurrence of commonly used pesticides in personal air samples and their associated health risk among paddy farmers. Sci. Total Environ., 603-604: 381-389.

Hatzilazarou SP, Charizopoulos ET, Papadopoulou-mourkidou E, Economou AS (2004) Dissipation of three organochlorine and four pyrethroid pesticides sprayed in a greenhouse environment during hydroponic cultivation of Gerbera. Pest Manag. Sci. 60(May): 1197–1204.

IARC (2020) The International Agency for Research on Cancer (IARC) is the specialized cancer agency of the World Health Organization. https://monographs.iarc.who.int/list-of-classifications.

Jacobsen-Pereira CH, Dos Santos CR, Maraslis FT, Pimentel L, Feijó, AJL, Silva CI, De Medeiros GS, Zeferino RC, Pedrosa CR, Maluf SW (2018) Markers of genotoxicity and oxidative stress in farmers exposed to pesticides. Ecotoxicol. Environ. Saf., 148: 177-183.

Jeder H, Laarif A, Chaieb I, Ksouri F (2018) Farmers' risk perceptions of pesticides used for greenhouses vegetables production in Tunisian Center-East. New Medit 17(4): 45–55.

Jeyaratnam, J (1990) Acute pesticide poisoning: A major global health problem.Health Stat. Q. 43: 139–44.

Juntarawijit C, Juntarawijit Y (2018) Association between diabetes and pesticides: A case-control study among Thai farmers. Environ Health Prev Med 23(1): 1–10.

Kah M, Beulke S, Tiede K, Hofmann T (2013) Nanopesticides: state of knowledge, environmental fate and exposure modelling. Crit Rev Environ Sci Technol 43:1823–1867.

Kah M (2015) Nanopesticides and nanofertilizers: emerging contaminants or opportunities for risk mitigation? Front. Chem. 3: 1-6.

Kim KH, Kabir E, Jahan SA (2017) Exposure to pesticides and the associated human health effects.Sci Total Environ 575: 525–535.

Kookana RS, Boxall AB, Reeves PT, Ashauer R, Beulke S, Chaudhry Q, Cornelis G, Fernandes TF, Gan J, Kah M, Lynch I, Ranville J, Sinclair C, Spurgeon D, Tiede K, Van den Brink PJ (2014) Nanopesticides: guiding principles for regulatory evaluation of environmental risks. J. Agric. Food Chem, 62(19): 4227-4240.

Lander F, Knudsen LE, Gamborg MO, Järventaus H, Norppa H. (2000) Chromosome aberrations in pesticide-exposed greenhouse workers. Scand. J. Work Environ. Health, 26 (5): 436–442.

Lewis KA, Tzilivakis J, Warner DJ, Green A (2016) An international database for pesticide risk assessments and management. Hum Ecol Risk Assess., 22(4): 1050–1064.

Macharia I (2015) Pesticides and health in vegetable production in Kenya. Biomed Res. Int. 2015.

MADR (2018) Ministère de l'Agriculture et du Développement Rural, Index des produits phytosanitaires à usage agricole, édition 2017. http://madrp.gov.dz/telecharger/gamme-des-produits-phytosanitaires-a-usage-agricole-homologues-index.

Mamane A, Baldi I, Tessier JF, Raherison C, Bouvier G (2015) Occupational exposure to pesticides and respiratory health. Eur Respir Rev., 24(136), 306-319.

Mengistie BT, Mol AP, Oosterveer P (2017) Pesticide use practices among smallholder vegetable farmers in Ethiopian Central Rift Valley. Environ. Dev. Sustain., 19(1), 301-324.

Mwabulambo SG, Mrema EJ, Vera Ngowi A, Mamuya S (2018) Health symptoms asssociated with pesticides exposure among flower and onion pesticide applicators in Arusha Region. Ann. Glob. Health 84(3): 369–379.

Nurcandra F, Mahkota R, Shivalli S(2018) Effect of personal protective equipment during pesticide application to neurological symptoms in farmers in Purworejodistrict, Indonesia. Kesmas 12(4): 165–171.

Ohayo-Mitoko GJA,Kromhout H, Simwa JM, Boleij JSM, Heederik D(2000) Self-reported symptoms and inhibition of acetylcholinesterase activity among kenyan agricultural workers. Occup Environ Med 57(3): 195–200.

Ojo J (2016) Pesticides use and health in Nigeria.IJS 18(4): 981-991–991.

Okonya JS, Kroschel J (2015) A cross-sectional study of pesticide use and knowledge of smallholder potato farmers in Uganda. Biomed Res. Int. 2015.

Palis FG, Flor RJ, Warburton H, Hossain M (2006) Our farmers at risk: behaviour and belief system in pesticide safety. J. Public Health, 28(1): 43-48.

Patel S, Sangeeta S (2019) Pesticides as the drivers of neuropsychotic diseases, cancers, and teratogenicity among agro-workers as well as general public. ESPR 26(1): 91–100.

Pesticide Properties Database (PPDB). https://sitem.herts.ac.uk/aeru/ppdb/en/index.htm.

Del Prado-Lu JL (2015) Insecticide residues in soil, water, and eggplant fruits and farmers' health effects due to exposure to pesticides. Environ Health Prev Med 20(1): 53–62.

Priyadharshini UK, Latha R, Kavitha U, Nirmala N (2017) Effects of organophosphorus pesticides on cardiorespiratory parameters among the farmers. JCDR, 11(9), 1-4.

Rahmoune H, Mimeche F, Guimeur K, Cherif K (2018) Utilisation des pesticides et perception des risques chez les agriculteurs de la région de Biskra (Sud Est d'Algérie). Int J Environ Stud.

Ramdani N, Tahri N, Belhadi A (2009) Pratiques phytosanitaires chez les serristes maraîchers des localités de Tolga et de Sidi-Okba (Wilaya de Biskra). JARA 8: 73–80.

Rehman H, Aziz AT, SagguS, Abbas ZK, Mohan A, Ansari AA (2014) Systematic review on pyrethroid toxicity with special reference to deltamethrin. JEZS 2(26): 60–70.

Remor AP, Totti CC, Moreira DA, Dutra GP, Heuser VD, Boeira JM (2009) Occupational exposure of farm workers to pesticides: biochemical parameters and evaluation of genotoxicity. Environ. Int. 35(2): 273–278.

Rezaei R, Damalas CA, Abdollahzadeh G (2018) Understanding farmers' safety behaviour towards pesticide exposure and other occupational risks: the case of Zanjan, Iran. Sci. Total Environ. 616–617: 1190–1198.

Roldán-Tapia L, Parrón T, Sánchez-Santed F(2005) Neuropsychological effects of long-term exposure to organophosphate pesticides.NeurotoxicolTeratol 27(2): 259–266.

Ross SMK, Mc Manus IC, Harrison V, Mason O (2013) Neurobehavioral problems following low-level exposure to organophosphate pesticides: a systematic and meta-analytic review. Crit. Rev. Toxicol. 43(1): 21–44.

Sánchez-Santed F, Colomina MT, Herrero Hernández E(2016) Organophosphate pesticide exposure and neurodegeneration. Cortex 74: 417–426.

Sharifzadeh MS, Damalas CA, Abdollahzadeh G (2017) Perceived usefulness of personal protective equipment in pesticide use predicts farmers' willingness to use it. Sci. Total Environ. 609: 517–23.

Slimani S, Boulakoud MS, Abdennour C (2011) Pesticide exposure and reproductive biomarkers among male farmers from north-east Algeria. Ann. Biol. Res.2(2): 290–97.

Slotkin TA (2004) Cholinergic systems in brain development and disruption by neurotoxicants: nicotine, environmental tobacco smoke, organophosphates. Toxicol. Appl. Pharmacol. 198(2): 132–151.

Son D, Somda I, Legreve A, Schiffers B (2017) Pratiques phytosanitaires des producteurs de tomates du burkinafaso et risques pour la santé et l'environnement. Cah. Agric. 26: 25005.

Sonchieu J, Ngassoum MB, Nantia AE, Laxman PS (2017) Pesticide Applications on Some Vegetables Cultivated and Health Implications in Santa, North West-Cameroon. IJAES. 4(2): 39–46.

Soudani N, Belhamra M,Ugya AY, Patel N, Carretta L, Cardinali A, Toumi K (2020) Environmental risk assessment of pesticide use in Algerian agriculture. J Appl Biol Biotechnol. 8(5): 36–47.

Soudani N, Belhamra M, Toumi K (2020) Pesticide use and risk perceptions for human health and the environment: a case study of Algerian farmers.IJSR 76(5): 10-28.

Stallones L, Beseler C (2002) Pesticide illness, farm practices, and neurological symptoms among farm residents in Colorado. Environ. Res., 90(2), 89-97.

Taira K (2014) Human neonicotinoids exposure in Japan. Jpn J Clin Eco 23(1): 14–24.

Ugwu JA, Omoloye AA, Asogwa EU, Aduloju AR (2015) Pesticide-handling practices among smallholder vegetable farmers in Oyo State, Nigeria. SCIRJ 3(4): 40–47.

US EPA Office of Pesticide Programs (2017) Chemicals evaluated for carcinogenic potential, annual cancer report 2017.

WHO (2010) World Health Organization, the WHO recommended classification of pesticides by hazard and guidelines to classification 2009. https://apps.who.int/iris/bitstream/handle/10665/44271/9789241547963_eng.pdf?sequence=1&isAllowed=y.

Yassin MM, Mourad TA, Safi JM (2002) Knowledge, attitude, practice, and toxicity symptoms associated with pesticide use among farm workers in the Gaza Strip. Occup Environ Med 59(6): 387–393.

Yarpuz-Bozdogan, N (2018) The importance of personal protective equipment in pesticide applications in agriculture. Curr Opin Environ Sci Health, 4: 1-4.