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Pesticides Residues in Weight Loss Dietary Supplements

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Abstract:
Background*: Dietary supplements (DSs) are products intended to enrich the diet. Worldwide DSs are categorised as food and regulated as food. However, most of the consumers of these products consider DSs as natural safe products which have the ability not only to enrich the diet but also to improve health. Nowadays DSs are involved in the nutrition of many people. Moreover, DSs are involved in the management of different health conditions although DSs are not medicines and differ from the pharmaceuticals in many aspects including regulation, safety testing, quality testing, etc. In the past 10 years many studies reported that more than 20% of the DSs worldwide have poor quality: contaminations, unproper labelling, undeclared pharmaceutical compounds, etc. This could be regarded as a natural consequence of the lack of obligatory analytical control for DSs worldwide. The aim of the present study was to analyze the content of pesticides residues in weight loss dietary supplements.*
Materials and Methods*: Twenty dietary supplements promoted for weight loss/obesity management were randomly selected. All samples were purchased form Bulgarian pharmacies and were labeled as herbal/natural dietary supplements. A screening for 127 pesticides was performed by a multimethod based on GC-MS/MS and LC-MS according to the guidelines of the European Standard for determination of pesticide residues in foods of plant origin (EN 15662:2018).*
Results*: Eight of the analyzed samples contained pesticides. The pesticides found were:Midacloprid, Carbendazim, Cypermethrin, lambda-Cyhalothrin, alpha-Hexachlorocyclohexane, Acetamiprid, Hexachlorobenzene, Procymidone, Dimethomorph, Chlorpyrifos, Thiophanate-methyl, Boscalid, Azoxystrobin, Tebuconazole, delta-Hexachlorocyclohexane, Acrinathrin.*
Conclusion: *Pesticides were found in 40% of the analyzed DSs. The results of the present study indicated an urgent need for obligatory monitoring of pesticides in DSs.*
Key Word*: Dietary supplements; Pesticides; Weight loss; Obesity; GC-MS; LC-MS.*

I. Introduction

Dietary supplements (DSs) are products regarded as sources of different important nutrients (vitamins, minerals) or other bioactive compounds which are used to enrich the diet [1]. Nowadays, the consumption of DSs has reached especially high levels [2][3]. The main key points for the fast and constant growth of the DSs consumption are liberal legislation, rapid and easy introduction of new DSs, easy purchases, advertisement, lifestyle trends. In general, most of the consumers associate these products with a healthy lifestyle model and safety.

However, nowadays the safety of DSs has become an important challenge: numerous cases of poor quality DSs, including contaminations with pharmacologically active compounds associated with serious adverse effects, unproper labeling, etc [3]. In general, more than 20% of the DS worldwide might have poor quality and might be dangerous for consumers [4] .

In the last years DSs used for weight management are one of the most popular and attractive DSs. At the same time these products are one of the most commonly contaminated DSs with undeclared compounds [3].

The aim of the present study was to analyze the content of pesticides residues in weight loss dietary supplements.

II. Material And Methods

Twenty dietary supplements used for weight loss/obesity management were randomly selected. All samples were purchased form Bulgarian pharmacies and were labeled as herbal/natural dietary supplements. A screening for 127 pesticides was performed by a multimethod based on GC-MS/MS and LC-MS according to the guidelines of the Bulgarian Institute for Standardization for the determination of pesticide residues in foods of plant origin (EN 15662:2018) [5][6]. All samples were stored in sterile containers prior to analysis. The weight of the samples required for the essay was 10 g. The sample preparation included homogenization, extraction with acetonitrile, centrifuging (for phase separation), a clean-up, acidificataion. The samples were analyzed by GC-MS/MS and LC-MS.

https://bds-bg.org/en/project/show/bds:proj:102689

III. Results

Pesticides were found in 8 of the analyzed samples (40% of the samples). The pesticides detected were: Imidacloprid, Carbendazim, Cypermethrin, lambda-Cyhalothrin, alpha-Hexachlorocyclohexane (alpha-HCH), Acetamiprid, Hexachlorobenzene, Procymidone, Dimethomorph, Chlorpyrifos, Thiophanate-methyl, Boscalid, Azoxystrobin, Tebuconazole, delta-Hexachlorocyclohexane (delta-HCH), Acrinathrin (table 1).

Carbendazim and Acetamiprid were one of the most commonly detected pesticides. Carbendazim was found in four samples and Acetamiprid was found in three of the samples. Three of the samples contained only one pesticide, 2 of the samples contained 2 different pesticides, 1 sample contained 3 different pesticides, and 2 of the samples contained more than 5 different pesticides. The presence of different pesticides in one product could have serious adverse effects and should be carefully regarded. At the same time DSs are products which could provide a long-term exposure to pesticides- normally these products are consumed for a long period of time (weeks, months).

Although in European Union (EU) DSs are regulated as food no data was found about the "Pesticide residue(s) and maximum residue levels (MRL)" for food/dietary supplements in EU. The data about the MRL (mg/kg) in food included fruits, nuts, vegetables, fungi, pulses, mosses and lichens, teas, coffee, herbal infusions, cocoa and carobs, hops, spices, honey, animal food products [7].

According to the EU legislation, MRL of 0.01 mg/kg is applied where a pesticide is not specifically mentioned [8].

The highest levels of pesticides residues were found in sample № 8: Hexachlorobenzene, Procymidone, Difenoconazole, Dimethomorph, Bifenthrin, Chlorpyrifos, Thiophanate-methyl, Imidacloprid, Carbendazim, Boscalid, Azoxystrobin, Acetamiprid. In this sample Carbendazim levels were the highest- 1,107 mg/kg. According to the EU legislation, MRL for Hexachlorobenzene in food from plant origin is 0,01 mg/kg and for herbs 0,02 mg/kg [9]. The levels of Hexachlorobenzene in this sample were 0,013 mg/kg. The daily intake of this DS is 1 g.

Some of the main characteristics of the detected pesticides are presented in table 2.

Table 1: Pesticides content in the analyzed weight loss dietary supplements

№	Description	Origin of the manufacturer	Formulation	Total weight of 1 capsule/ tablet in mg	Recommended daily intake according to the label of the product	Pesticides content (mg/ kg)
1	Garcinia cambogia extract	European Union	Capsules	570	Up to 4 capsules per day (1-2 capsules/ 2 times per day).	-
2	Green tea extract	European Union	Capsules	340	4 capsules per day (2 capsules/ 2 times per day)	-
3	Green tea extract	European Union	Tablets	190	6 tablets per day (2 tablets/ 3 times per day)	-
4	Combination- different plant extracts	European Union	Capsules	450	2 capsules per day (1 capsule/2 times per day)	Imidacloprid (0,017) Carbendazim (0,011)
5	Green tea extract	USA	Capsules	500	2 capsules per day (1 capsule/2 times per day)	Cypermethrin (0,047) Lambda-cyhalothrin (0,018) Alpha-HCH (0,013) Carbendazim (0,016) Imidacloprid (0,034) Acetamiprid (0,044)
6	Green tea extract	USA	Capsules	430	1 capsule daily	Acetamiprid (0,025)
7	Green coffee extract	European Union	Capsules	500	2 capsules per day (1 capsule/2 times per day)	Lambda-cyhalothrin (0,188)

8	Combination-different plant extracts	European Union	Capsules	500	2 capsules per day (1 capsule/2 times per day)	Hexachlorobenzene (0,013) Procymidone (0,055) Difenoconazole (0,119) Dimethomorph (0,035) Bifenthrin (0,015) Chlorpyrifos (0,013) Thiophanate-methyl (0,159) Imidacloprid (0,015) Carbendazim (1,107) Boscalid (0,043) Azoxystrobin (0,023) Acetamiprid (0,029)
9	Yohimbine	USA	Capsules	900	2 capsules daily (1 capsule/ 2 times per day)	-
10	Garcinia cambogia extract	USA	Tablets	1500	Up to 4 capsules per day (1-2 capsules/ 2 times per day).	-
11	Combination-plant extracts	European Union	Capsules	450	2 capsules per day (1 capsule/2 times per day)	-
12	Biotin	Canada	Tablets	220	2 tablets daily (1 tablet /2 times per day)	-
13	Combination-plant extracts	China	Capsules	300	2 capsules per day (1 capsule/2 times per day)	-
14	Guarana extract	European Union	Tablets	900	8 tablets per day (2 tablets/ 4 times per day)	Tebuconazole (0,022)
15	Combination-plant extracts	European Union	Capsules	400	2 capsules per day (1 capsule/2 times per day)	alpha-HCH (0,020) delta-HCH (0,017)
16	Combination-plant extracts	European Union	Capsules	500	2 capsules per day (1 capsule/2 times per day)	-
17	Combination-plant extracts	European Union	Tablets	500	Up to 3 tablets per day (1 tablet/2 or 3 times per day)	Lambda-cyhalothrin (0,016) Acrinathrin (0,082) Carbendazim (0,128)
18	Combination-plant extracts	European Union	Capsules	450	2 capsules per day (1 capsule/2 times per day)	-
19	Combination-plant extracts	USA	Capsules	550	2 capsules per day	-
20	Combination-plant extracts	European Union	Capsules	800	2 capsules per day (1 capsule/2 times per day)	-

Table 2: Main characteristics of the detected pesticides

Pesticide	Description	Application	Toxicity
Acetamiprid	Alpha-chloro-N-heteroaromatic compound. Agonist of nicotinic acetylcholine receptors.	Insecticide	Hepatorenal, immunological, neurological, genotoxic, and reproductive adverse effects [10].
Acrinathrin	A cyclopropanecarboxylate ester. Disrupts the nervous system of insects.	Insecticide	Decreasement of body weight gain, skin lesions [11].

alpha-HCH	An isomer of hexachlorocyclohexane.	Insecticide	Human carcinogen [12], [13].
Azoxystrobin	Inhibitor of mitochondrial respiration	Fungicide	Neurotoxicity [14] . Reproductive toxicity in fish [15].
Boscalid	A succinate dehydrogenase inhibitor [16].	Fungicide	A short-term exposure is associated with mitochondrial dysfunction in human cells [16].
Bifenthrin	A synthetic pyrethroid, associated with a broad spectrum of insecticidal and acaricidal activity [17].	Insecticide	Acute lethal effects to aquatic species. Nonlethal negative impacts on different non-target organisms. Immune toxicity. Reproductive toxicity and endocrine disruption effects [18].
Carbendazim	A benzimidazole fungicide.	Fungicide	Embryotoxicity, teratogenic effects, infertility, hepatocellular dysfunction, endocrine-disrupting effects, hematological adverse effects, mutagenic effects [19].
Chlorpyrifos	An organophosphate pesticide. It inhibits the acetylcholinesterase. Chlorpyrifos causes disruption of the nervous system and death of the animal organism [20].	Insecticide	Adverse effects in animals and humans: endocrine disruption, neurotoxicity, reproductive toxicity, carcinogenesis [21].
delta-HCH	An isomer of hexachlorocyclohexane.	Insecticide	Endocrine toxicity [22].
Difenoconazole	A broad-spectrum triazole fungicide [23]. It is a steroid demethylation inhibitor and affects mainly on the vegetative stage of fungi [24].	Fungicide	Irritant to skin and mucous membranes [23]
Dimethomorph	Dimethomorph represents a mixture of approximately equal amounts of two geometrical isomers (*E*- and *Z*-isomers) [25].	Fungicide	Liver damage.
Hexachlorobenzene	A fungicide with molecular formula C_6Cl_6.	Fungicide	Long-term exposure can cause liver damage and reproductive toxicity. Accumulates in body fat [26]. It is regarded as a probable human carcinogen.
Imidacloprid	Belongs to the neonicotinoids' family. It acts on the central nervous system of insects.	Insecticide	Reproductive toxicity [27].
lambda-Cyhalothrin	A pesticide which belongs to the Pyrethroid's family.	Insecticide	Pancreatic toxicity [28].
Thiophanate-methyl	A widely used fungicide. The compound exhibit high mobility in soil [29].	Fungicide	Hepatotoxicity, kidney toxicity [30], [31].
Tebuconazole	A triazole fungicide.	Fungicide	Tebuconazole could reduce cell viability and disturb normal cell cycle [32].

IV. Discussion

EU strictly regulates the use of plant protection products. In EU a plant protection product can be used only if it covers the following important key points: no harmful effects on humans (consumers, farmers, bystanders, etc.), no unacceptable consequences on the environment and to be sufficiently effective [33].

Although pesticides are considered as compounds of great importance for the agriculture these chemicals are also regarded as dangerous pollutants which can cause serious consequences for health and ecosystems [10].

For example, Acetamiprid is a chloronicotinyl insecticide which is designed as nicotinic acetylcholine receptor agonist in insects [10]. However, exposure to acetamiprid is associated with adverse effects in non-targeted organisms as well including mammals. Its toxic metabolites are detected in the liver, brain, plasma and urine mammals. The effects of acetamiprid exposure lead to hematological and biochemical changes resulting in serious hepatorenal, immunological, neurological, genotoxic and reproductive adverse effects [10]. Acetamiprid was found in three of the analyzed DSs.

Another insecticide, which was found in two of the analyzed samples, alpha-HCH is regarded as a carcinogen [13]. Its long-term exposure was associated with hyperplastic nodules and carcinomas in the livers of rats and mice [13]. Adeoluwa Oluwaseyi Adeleye and coworkers reported a study which results indicated that consumption of food contaminated with alpha-HCH could pose a carcinogenic risk for adults and children [12].

Carbendazim which was found in four of the analyzed samples is regarded as one of the major pollutants which can be detected in food, soil, and water. Its long-term exposure is associated with acute or delayed toxic effects on invertebrates, aquatic life forms, soil microorganisms and humans [19].

Hexachlorobenzene, found in sample № 8, was listed under the Stockholm Convention is considered as another dangerous organic pollutant. It is associated the following characteristics: long-range environment transport, persistence, bioaccumulation, and toxicity [34].

Humans' exposure to pesticides should be carefully regarded. Sources of pesticides could be food, dietary supplements, water, or the environment. The long-term exposure to pesticides is especially dangerous. In general, DS are products which are taken for a long period of time (weeks, months, etc.) and could provide a long-term exposure to dangerous compounds. Poor quality DSs would not enrich the diet and improve health but could cause serious adverse effects. Moreover, DSs are products which are consumed by people from different age and health conditions.

The quality of DSs should be carefully monitored including quality and quantity control of the active ingredients, screening for undeclared compounds, screening for lead levels and obligatory screening for pesticides. There is an urgent need for strict enforcement of regulations on DSs to minimize human health risks. Novel regulations about MRL in DSs in EU would be especially beneficial for ensuring the consumers safety.

V. Conclusion

The results of the present study indicated an urgent need for monitoring of pesticides in DSs. Pesticides were found in 40% of the analyzed DSs. In this study Carbendazim and Acetamiprid were one of the most commonly detected pesticides. Carbendazim was found in four samples and Acetamiprid was found in three of the samples. Three of the samples contained only one pesticide, two of the samples contained two different pesticides, one sample contained three different pesticides and two of the samples contained more than five different pesticides. The presence of different pesticides in one product could have serious adverse effects and should be carefully regarded. Something more, DSs could provide a long-term exposure to pesticides, because these products are normally consumed for a long period of time.

References

1. M. Bensa, I. Vovk, and V. Glavnik, "Resveratrol Food Supplement Products and the Challenges of Accurate Label Information to Ensure Food Safety for Consumers," Nutrients, vol. 15, no. 2, p. 474, Jan. 2023, doi: 10.3390/nu15020474.
2. J. Blumberg, B. Frei, V. Fulgoni, C. Weaver, and S. Zeisel, "Contribution of Dietary Supplements to Nutritional Adequacy in Various Adult Age Groups," Nutrients, vol. 9, no. 12, p. 1325, Dec. 2017, doi: 10.3390/nu9121325.

3. V. R. Kozhuharov, K. Ivanov, D. Karcheva-Bahchevanska, N. Prissadova, and S. Ivanova, "Development and Validation of Gas Chromatography–Mass Spectrometry Method for Quantification of Sibutramine in Dietary Supplements," Processes, vol. 11, no. 8, p. 2337, Aug. 2023, doi: 10.3390/pr11082337.
4. V. R. Kozhuharov, K. Ivanov, and S. Ivanova, "Dietary Supplements as Source of Unintentional Doping," BioMed Res. Int., vol. 2022, pp. 1–18, Apr. 2022, doi: 10.1155/2022/8387271.
5. https://www.en-standard.eu/csn-en-15662-foods-of-plant-origin-multimethod-for-the-determination-of-pesticide-residues-using-gc-and-lc-based-analysis-following-acetonitrile-extraction-partitioning-and-clean-up-by-dispersive-spe-modular-quechers-method/
6. https://bds-bg.org/en/project/show/bds:proj:102689.
7. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/mrls/details?lg_code=EN&pest_res_id_list=38&product_id_list=
8. https://food.ec.europa.eu/plants/pesticides/maximum-residue-levels/eu-legislation-mrls_en#:~:text=A%20general%20default%20MRL%20of,e.g.%20babies%2C%20children%20and%20vegetarians
9. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/mrls/details?lg_code=EN&pest_res_id_list=122&product_id_list=
10. A. Phogat, J. Singh, V. Kumar, and V. Malik, "Toxicity of the acetamiprid insecticide for mammals: a review," Environ. Chem. Lett., vol. 20, no. 2, pp. 1453–1478, Apr. 2022, doi: 10.1007/s10311-021-01353-1.
11. Market Development, AgrEvo Japan Limited, Summary of Toxicological Studies on Acrinathrin, J. Pesticide Sci. 23, 206-212, 1998
12. A. O. Adeleye, M. B. Sosan, and J. A. O. Oyekunle, "Occurrence and Human Health Risk of Dichlorodiphenyltrichloroethane (DDT) and Hexachlorocyclohexane (HCH) Pesticide Residues in Commonly Consumed Vegetables in Southwestern Nigeria," J. Health Pollut., vol. 9, no. 23, p. 190909, Sep. 2019, doi: 10.5696/2156-9614-9.23.190909.
13. A. E. Bradley, J. L. Shoenfelt, and J. L. Durda, "Carcinogenicity and mode of action evaluation for alpha-hexachlorocyclohexane: Implications for human health risk assessment," Regul. Toxicol. Pharmacol., vol. 76, pp. 152–173, Apr. 2016, doi: 10.1016/j.yrtph.2015.12.007.
14. K. Nguyen et al., "Neurotoxicity assessment of QoI strobilurin fungicides azoxystrobin and trifloxystrobin in human SH-SY5Y neuroblastoma cells: Insights from lipidomics and mitochondrial bioenergetics," NeuroToxicology, vol. 91, pp. 290–304, Jul. 2022, doi: 10.1016/j.neuro.2022.06.002.
15. F. Cao, L. Zhu, H. Li, S. Yu, C. Wang, and L. Qiu, "Reproductive toxicity of azoxystrobin to adult zebrafish (Danio rerio)," Environ. Pollut., vol. 219, pp. 1109–1121, Dec. 2016, doi: 10.1016/j.envpol.2016.09.015.
16. D. d'Hose, P. Isenborghs, D. Brusa, B. F. Jordan, and B. Gallez, "The Short-Term Exposure to SDHI Fungicides Boscalid and Bixafen Induces a Mitochondrial Dysfunction in Selective Human Cell Lines," Molecules, vol. 26, no. 19, p. 5842, Sep. 2021, doi: 10.3390/molecules26195842.
17. I. Sadowska-Woda, D. Popowicz, and A. Karowicz-Bilińska, "Bifenthrin-induced oxidative stress in human erythrocytes in vitro and protective effect of selected flavonols," Toxicol. In Vitro, vol. 24, no. 2, pp. 460–464, Mar. 2010, doi: 10.1016/j.tiv.2009.09.024.
18. Y. Yang, N. Wu, and C. Wang, "Toxicity of the pyrethroid bifenthrin insecticide," Environ. Chem. Lett., vol. 16, no. 4, pp. 1377–1391, Dec. 2018, doi: 10.1007/s10311-018-0765-0.
19. S. Singh et al., "Toxicity, monitoring and biodegradation of the fungicide carbendazim," Environ. Chem. Lett., vol. 14, no. 3, pp. 317–329, Sep. 2016, doi: 10.1007/s10311-016-0566-2.
20. J. P. Giesy and K. R. Solomon, Eds., Ecological Risk Assessment for Chlorpyrifos in Terrestrial and Aquatic Systems in the United States, vol. 231. in Reviews of Environmental Contamination and Toxicology, vol. 231. Cham: Springer International Publishing, 2014. doi: 10.1007/978-3-319-03865-0.
21. H. Ubaid Ur Rahman, W. Asghar, W. Nazir, M. A. Sandhu, A. Ahmed, and N. Khalid, "A comprehensive review on chlorpyrifos toxicity with special reference to endocrine disruption: Evidence of mechanisms, exposures and mitigation strategies," Sci. Total Environ., vol. 755, p. 142649, Feb. 2021, doi: 10.1016/j.scitotenv.2020.142649.
22. J. Olivero-Verbel, A. Guerrero-Castilla, and N. R. Ramos, "Biochemical Effects Induced by the Hexachlorocyclohexanes," in Reviews of Environmental Contamination and Toxicology Volume 212, D. M. Whitacre, Ed., in Reviews of Environmental Contamination and Toxicology, vol. 212. New York, NY: Springer New York, 2011, pp. 1–28. doi: 10.1007/978-1-4419-8453-1_1.
23. R. Liu, J. Li, L. Zhang, T. Feng, Z. Zhang, and B. Zhang, "Fungicide Difenoconazole Induced Biochemical and Developmental Toxicity in Wheat (Triticum aestivum L.)," Plants, vol. 10, no. 11, p. 2304, Oct. 2021, doi: 10.3390/plants10112304.
24. S. H. Abd-Alrahman et al., "Exposure to difenoconazole, diclofop-methyl alone and combination alters oxidative stress and biochemical parameters in albino rats," Int. J. Clin. Exp. Med., vol. 7, no. 10, pp. 3637–3646, 2014.
25. EFSA (European Food Safety Authority), Alvarez, F, Arena, M, Auteri, D, Binaglia, M, Castoldi, AF, Chiusolo, A, Colagiorgi, A, Colas, M, Crivellente, F, De Lentdecker, C, De Magistris, I, Egsmose, M,

Fait, G, Ferilli, F, Gouliarmou, V, Halling, K, Nogareda, LH, Ippolito, A, Istace, F, Jarrah, S, Kardassi, D, Kienzler, A, Lanzoni, A, Lava, R, Leuschner, R, Linguadoca, A, Lythgo, C, Magrans, O, Mangas, I, Miron, I, Molnar, T, Padovani, L, Panzarea, M, Parra Morte, JM, Rizzuto, S, Serafimova, R, Sharp, R, Szentes, C, Szoradi, A, Terron, A, Theobald, A, Tiramani, M, Vianello, G and Villamar-Bouza, "Conclusion on the peer review of the pesticide risk assessment of the active substance dimethomorph," EFSA Journal 2023, vol. 21, no. 6, p. 8032, doi: https://doi.org/10.2903/j.efsa.2023.8032.

26. E. M. Udarbe Zamora, "Hexachlorobenzene," in Encyclopedia of Toxicology, Elsevier, 2014, pp. 869–871. doi: 10.1016/B978-0-12-386454-3.00150-0.
27. R. Bal et al., "Assessment of imidacloprid toxicity on reproductive organ system of adult male rats," J. Environ. Sci. Health Part B, vol. 47, no. 5, pp. 434–444, May 2012, doi: 10.1080/03601234.2012.663311.
28. S. Sakr and W. A. Rashad, "Lambda-cyhalothrin-induced pancreatic toxicity in adult albino rats," Sci. Rep., vol. 13, no. 1, p. 11562, Jul. 2023, doi: 10.1038/s41598-023-38661-1.
29. European Food Safety Authority (EFSA) et al., "Peer review of the pesticide risk assessment of the active substance thiophanate-methyl," EFSA J., vol. 16, no. 1, Jan. 2018, doi: 10.2903/j.efsa.2018.5133.
30. K. Jia et al., "Thiophanate-methyl induces severe hepatotoxicity in zebrafish," Chemosphere, vol. 248, p. 125941, Jun. 2020, doi: 10.1016/j.chemosphere.2020.125941.
31. A. Feki et al., "Methyl thiophanate-induced toxicity in liver and kidney of adult rats: a biochemical, molecular and histopathological approach," Cell. Mol. Biol., vol. 63, no. 2, p. 20, Feb. 2017, doi: 10.14715/cmb/2017.63.2.4.
32. J. Zhou, J. Zhang, F. Li, and J. Liu, "Triazole fungicide tebuconazole disrupts human placental trophoblast cell functions," J. Hazard. Mater., vol. 308, pp. 294–302, May 2016, doi: 10.1016/j.jhazmat.2016.01.055.
33. https://food.ec.europa.eu/system/files/2016-10/pesticides_mrl_legis_factsheet_en.pdf
34. G. Wang et al., "Hexachlorobenzene sources, levels and human exposure in the environment of China," Environ. Int., vol. 36, no. 1, pp. 122–130, Jan. 2010, doi: 10.1016/j.envint.2009.08.005.