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Methoxychlor (MXC) in Food

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Executive Summary

Methoxychlor (MXC) is an organochlorine pesticide primarily used as an insecticide against pests on crops and livestock. It is persistent in the environment and has a strong potential for long-range environmental transportation. MXC has a potential to bioaccumulate in fishes; while in human, it is quickly metabolized by demethylation to form phenolic metabolites which are then eliminated from the body, and therefore MXC is not bioaccumulated.

2. MXC is not genotoxic and not carcinogenic in experimental animals. In experimental mammals, the acute toxicity from oral exposure to MXC is low. The main targets for the chronic toxicity of MXC are the nervous, endocrine and reproductive systems.

3. The Joint Food and Agriculture Organization (FAO)/ World Health Organization (WHO) Meeting on Pesticide residues (JMPR) has evaluated the toxicity of MXC in food in 1965 and 1977. JMPR has allocated an acceptable daily intake (ADI) of 0 – 100 μg/kg body weight (bw) for MXC.

4. This study serves (i) to determine the level of MXC in foods available in the local market; (ii) to estimate the dietary exposure to MXC of the Hong Kong adult population; and (iii) to assess the associated health risk.

Methods

5. A total of 300 individual samples (correspond to 100 food items) were collected locally. The samples were chosen mainly based on their local popularity, reported MXC levels in the literature, and availability in

the local market. These samples were classified into 14 different food groups, including “Cereals and grains products”, “Vegetables”, “Fruits”, “Nuts and seeds”, “Meats and offals”, “Eggs and egg products”, “Milk and dairy products”, “Fish”, “Fish products”, “Crustaceans and molluscs”, “Fats and oils”, “Beverages”, “Herbs and spices” and “Honey”.

Results

6. All samples were not detected with MXC. In the chemical testing of this study, the limit of detection (LOD) for MXC was 0.1 µg/kg.

7. The lower-bound (LB) and upper-bound (UB) mean concentration of MXC in all samples were 0 and 0.1 µg/kg, respectively.

8. Regarding the dietary exposure to MXC of the local adult population, the LB and UB exposure estimates of MXC for average consumers are 0 and 0.002283 µg/kg bw/day respectively, while for high consumers (90th percentile), the LB and UB exposure estimates are 0 and 0.003608 µg/kg bw/day respectively. These dietary exposures are much lower than 100 µg/kg bw/day, indicating that the adverse health effects for average and high consumers of the population due to MXC upon usual consumption of food are unlikely.

9. Since the results for all samples were below the LOD, the actual food group contribution to the overall MXC exposure was not reflected.

Conclusion and Recommendations

10. In this study, all samples were not detected with MXC, with the

LOD of 0.1 μg/kg. The estimated dietary exposures to MXC for the Hong Kong adult population indicate that the current dietary exposure to MXC for the Hong Kong adult population does not raise a health concern.

11. In Hong Kong, the Pesticide Residues including MXC residues in food is regulated by the Pesticide Residues in Food Regulation (Cap. 132CM). For pesticide residues with no specified MRLs/EMRLs in Schedule 1 in the Regulation, the Regulation stipulates that except for exempted pesticides, import or sale of food containing such pesticide residues is allowed if the consumption of the food concerned is not dangerous or prejudicial to health based on risk assessment conducted by the Centre for Food Safety (CFS). CFS has been closely monitoring the latest international development of regulatory control and will review the regulatory standard, as necessary and appropriate.

12. The findings of the dietary exposure to MXC in the present study do not warrant changes to the basic dietary advice on healthy eating. The public is advised to maintain a balanced and varied diet which includes a wide variety of fruits and vegetables.

Risk Assessment Studies –

Methoxychlor (MXC) in Food

Objectives

This study aims (i) to determine the level of methoxychlor (MXC) in foods available in the local market; (ii) to estimate the dietary exposure to MXC of the Hong Kong adult population; and (iii) to assess the associated health risk.

Background

2. Methoxychlor (MXC) is an organochlorine pesticide (OCP) which has been used as a replacement for dichlorodiphenyltrichloroethane (DDT), a structural analogue (Figure 1).[1] Their mode of action are sodium channel modulators, whereas MXC is less persistent in the environment and less toxic to human, when compared with DDT. Furthermore, MXC does not accumulate in the mammals as DDT does.[2,3]

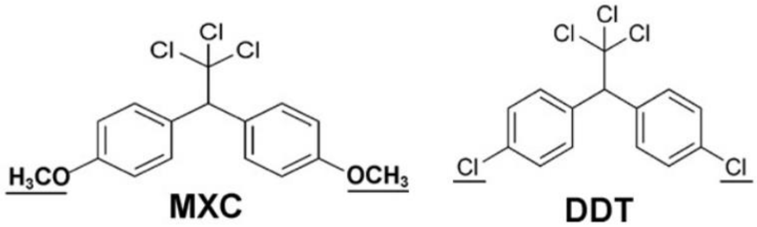

Figure 1. General structures of MXC and DDT. The underlined chlorine atoms in DDT are replaced with the underlined methoxy groups in MXC.

3. MXC is primarily used as an insecticide against a wide range of pests, including houseflies and mosquitos, cockroaches, chiggers, and various arthropods commonly found on field crops, vegetables, fruits, stored grain, livestock, and domestic pets. It is usually dissolved in a petroleum-based liquid and applied as a spray. MXC does not occur naturally in the environment. It is released to the environment mainly as a result of its application to crops and livestock as a pesticide.[1,4]

4. Although MXC is less persistent than DDT in the environment, its residue in soils and sediments is still of concern. Besides, MXC has a strong potential for long-range environmental transport. MXC has not only been detected in the environment including in urban cities, rural areas and in regions that used MXC as a pesticide in agricultural activities, but has also been found in the Arctic and Antarctic regions far away from any sources of release. In addition, MXC is toxic to aquatic animals and has a potential to bioaccumulate in fishes. MXC and its metabolites also cause endocrine disrupting effects targeting reproduction in experimental animals.[1]

5. Due to the concerns about the effects of MXC on human health and the environment, the uses of MXC as a pesticide had been suspended in many places including the United States (US) and European Union (EU) member states in the 2000s.[1,5] In 2021, the Persistent Organic Pollutants Review Committee (POPRC) of the Stockholm Convention on Persistent Organic Pollutants under the United Nation Environment Programme (UNEP) reported that MXC is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects such that global action is warranted.[6]

Occurrence in Food

6. Exposure of the general population to MXC can take place by consumption of contaminated food and drinking water.[1,7]

7. MXC was detected in different food including dairy products, cereals and grain products, vegetables, fruits. According to the analysis of European Food Safety Authority (EFSA) in 2018, MXC was quantified in one equine fat sample as well as four coffee bean samples imported from Brazil, Ethiopia, Peru and Uganda at the concentrations in the range of 10 – 50 µg/kg (LOQ of 10 µg/kg). It was concluded that the acute dietary exposure to MXC, would not be expected to pose a concern to consumer health.[1,8]

8. The levels of OCP residues in 3 different vegetables: lettuce, onion and cabbage from farms in Kumasi, Ghana in September 2014 were studied. Mean concentrations of MXC in the vegetables were in the range of 9 – 184 µg/kg. The measured concentrations were higher than the EU Maximum Residue Limits (MRL) of 10 µg/kg for these vegetables. However, rather than being based on specific risks, the EU MRL for MXC is based on the default lowest limit of analytical determination in EU law. The estimated daily intakes of MXC resulting from the levels measured in vegetables did not exceed an acceptable daily intake (ADI) of 5 µg/kg/day established by the US EPA. Therefore, the levels reported did not result in identified risks to the population.[9]

9. In another study, concentration of MXC in amaranth and fluted pumpkin collected in November 2017 to January 2018 in southwestern Nigeria was investigated. The mean concentration of MXC in amaranth was 4590±2774 µg/kg dry weight and 6223±2489 µg/kg dry weight in fluted pumpkin. Based on the reference dose for reproductive and

developmental effects (RfD) of 5 µg/kg/day, it was estimated a potential risk for consumers for these vegetables. The use of contaminated water from the river by farmers might contribute to the OCP residues detected in the vegetables, such that the contamination can come from the soil on which the vegetables were planted or from long-range transportation of the OCPs applied to crops elsewhere.[10]

10. According to the report of POPRC issued in 2021, MXC has been found in surface water, groundwater and drinking-water. MXC has been detected in surface waterbodies in Europe and Canada, and in French groundwaters, years after it was phased out. MXC has also been detected in an Arctic lake and surface seawater in a region covering the North Pacific to the Arctic Ocean and in the drinking water from Slovakia. For people who consume large amounts of fish and seafood from MXC-contaminated waters, their exposure to MXC from food may be elevated.[1]

Toxicity

11. The health effects of MXC have been investigated mainly in studies using technical grade MXC. Technical grade MXC typically contains about 80–90% MXC, with the remainder being composed of more than 50 related compounds.[4]

Toxicokinetics

12. In experimental mammals, orally administered MXC are absorbed and distributed in different tissues, with the highest levels of MXC usually found in fat. MXC is metabolised rapidly by the liver and neither the parent compound nor the metabolites tend to accumulate in fat or other tissue. The major pathway by which MXC is metabolized is demethylation to

form phenolic metabolites, with dechlorination and dehydrochlorination reactions occurring to a lesser extent. Most of the ingested dose is eliminated in the feces, and therefore MXC is not accumulated. The toxicokinetics of MXC in humans is expected to be similar to the toxicokinetics of MXC observed in experimental mammals.[1,4]

Acute toxicity

13. Acute toxicity from oral exposure to MXC is low. The oral LD_{50} is larger than 3,000,000 µg/kg bw in rats.[11,12] In experimental mammals, mild liver effects have been reported upon oral exposure to MXC. Symptoms of high acute exposure include central nervous system depression, progressive weakness and diarrhea.[13]

Chronic toxicity

14. MXC is not genotoxic and not carcinogenic in experimental animals. Chronic oral exposure to MXC has resulted in effects to the liver, kidneys, body weight and nervous system in the experimental mammals.[13] Toxicological studies have showed that MXC possibly produce neurological effect, cause endocrine disruption as well as adversely affect the reproductive system.[1,7,14]

Nervous system

15. Animal studies have showed that higher levels of exposure to MXC can produce neurological effects, such as apprehension, nervousness, increased salivation, decreased locomotor activity, tremors, convulsions and death. The reported $LOAEL_{oral}$ values in rats are 2,500,000 µg/kg/day for decreased locomotor activity and 3,000,000 µg/kg/day for tremors.[4] In people with compromised liver function, neurological signs may occur at lower MXC exposure levels. MXC has been demonstrated to be a

neurotoxicant even in the absence of metabolic transformation.[1]

Endocrine system and reproduction system

16. MXC can be metabolized in *vivo* into two demethylated compounds (2,2-bis-(p-hydroxyphenyl)-1,1,1-trichloroethane (HPTE) and 2,2-bis-(p-hydroxyphenyl)-1,1,1-dichloroethane (HPDE)) and two O-ring methylated compounds. These metabolites bind to the estrogen and androgen receptors. Therefore, MXC may impair reproductive function.[1,5,15]

17. According to the study about the effects of MXC on female rhesus monkeys during peripubertal period, MXC can increase estrogen activity of serum and lead to premature emergence of a secondary sex characteristic, reddening and swelling of skin, retarded growth of the nipple, as well as increased incidence of ovarian cysts/masses after an 8-month recovery period.[16]

18. In rabbits orally exposed to methoxychlor, excessive loss of litters (abortions) was observed. Skeletal effects have been observed in the offspring of rats exposed to MXC by gavage. In addition, it has been reported that the long-term oral exposure to MXC can increase fetotoxicity in animals, as well as affect the reproductive development and reduce the fertility of offspring.[13] Animal and *in vitro* studies have suggested that MXC may adversely affect the development, histopathology, and function of the human reproductive system. Observed reproductive effects are indicative of interference with the normal actions of estrogen or androgen.[1]

Epidemiological studies

19. Epidemiological studies have suggested possible associations between MXC exposure and leukemia as well as between MXC exposure

and breast cancer incidence. However, definitive conclusions on these relationships are not possible due to exposure to multiple pesticides and multiple risk factors.[1]

20. A epidemiology study about adults in Brazil found differential effects on males and females associated with OCPs exposure has showed that the higher concentrations of MXC exposure are significantly associated with increased total T3 levels in women. The detection of MXC in the serum of men are associated with a statistically significantly increased odds of having TPOAb levels greater than 10 U/mL, whereas TPOAb levels may be a useful indicator of thyroid injury or inflammation.[1,17]

Health-based Guidance Value

21. The Joint Food and Agriculture Organization (FAO)/ World Health Organization (WHO) Meeting on Pesticide residues (JMPR) has evaluated the toxicity of MXC in 1965 and 1977.[11,12]

22. JMPR has allocated an acceptable daily intake (ADI) of 0 – 100 μg/kg bw for MXC.[11,12]

Regulatory Control

Codex Alimentarius Commission (Codex)

23. Codex has not established Maximum Residue Limits/ Extraneous Maximum Residue Limits (MRLs/EMRLs) for MXC in food.

EU

24. In EU, MXC has not been approved as an active substance for plant protection products in 2002. The authorisations for plant protection products containing MXC has been withdrawal since 2003.

25. According to Commission Regulation (EC) No 149/2008, there are some 370 EU MRLs, including 10 μg/kg for MXC in fresh fruits, vegetables, nuts and fungi, as well as 100 μg/kg for MXC in teas, hops and spices. Notably, the EU MRL for MXC is based on the default lowest limit of analytical determination, rather than based on specific risks.[1,18]

US

26. According to the Methoxychlor Reregistration Eligibility Decision (RED) in 2004, the US Environmental Protection Agency (EPA) has determined that MXC is not eligible for reregistration. All registered technical sources of MXC were canceled in 2003, and all tolerances have been revoked.[1,5]

27. The US has previously established 79 tolerances of 1000 – 100,000 μg/kg for MXC in agricultural products. All tolerances for MXC residues have been revoked in 2002 since all registrations of pesticides containing MXC are suspended or canceled, and there are insufficient data to find the pesticide safe. The US EPA has also determined that it is not necessary to assess the risks of MXC products because there are no tolerances for MXC and all of the remaining products have been suspended.[5,19]

Australia

28. In Australia, the only MXC product registration was discontinued

in 1987. According to the Agricultural and Veterinary Chemicals Code (MRL Standard) Instrument 2019 that shows the text of the law as amended and in force on 20 January 2023, there is an extraneous residue limit (ERL) of 1000 μg/kg for MXC in primary feed commodities, whereas ERL refers to a pesticide residue arising from environmental sources (including former agricultural uses) other than the use of the chemical directly or indirectly on the food, agricultural commodity or animal feed.[1,20]

Mainland China

29. The registration of MXC as a pesticide has been stopped in the Mainland China since 1990s. According to the National food safety standard—Maximum residue limits for pesticides in food (GB 2763-2021), there are some 30 MRLs of 10 μg/kg for MXC in various food items including fresh fruits, vegetables and nuts.[1,21]

Other countries

30. MXC is no longer registered for use in places including Norway and Canada in 2000s. The use of MXC as an insecticide has been banned in Belarus and Egypt in 1990s. Monaco, Qatar, the Republic of Korea, the State of Palestine, Thailand and Costa Rica do not currently use MXC. In addition, MXC has also been banned in Turkey, Guinea, Indonesia, Mauritania, Oman, Saudi Arabia and in Ghana. In Mexico, MXC is a restricted pesticide than can only be used under the supervision of trained and authorized personnel since August 1991.[1]

31. In January 2022, POPRC decided to recommend to the Conference of the Parties that it consider listing MXC in Annex A to the Stockholm Convention without specific exemptions. The Convention is a global treaty to protect human health and the environment from chemicals

that remain intact in the environment for long periods, become widely distributed geographically, accumulate in the fatty tissue of humans and wildlife, and have harmful impacts on human health or on the environment. Once MXC is listed under Stockholm Convention, parties of the Convention must take measures to eliminate the production and use of MXC.[22]

Local situation

32. In Hong Kong, the handling of pesticides is regulated by the Pesticides Ordinance (Cap. 133). Under the Ordinance, only pesticides that have been registered in Hong Kong may be distributed in accordance with a Pesticides License and used in Hong Kong. Individual products do not have to be registered as long as they contain the registered active ingredient and conform to the specified maximum concentration of active ingredient(s) and permitted formulation detailed in the Pesticides Register.

33. The Pesticides Register is in two parts. Pesticides registered in Part I are ready-for-use domestic pesticides and those in Part II are all other pesticides. Currently, MXC is listed as the active ingredient in Part I of the Pesticides Register. The permitted formulation and maximum concentration for supply and retail sale for MXC are aerosol dispenser and 3% weight by volume, respectively.[23]

34. Since 1 August 2014, the Pesticide Residues in Food Regulation (Cap. 132CM) has come into operation. The Regulation aims to enhance regulatory control of pesticide residues in food to protect public health. The Regulation specifies in Schedule 1 a list of MRLs/EMRLs for certain pesticide-food pairs, i.e. the maximum concentration of specified pesticide residues permitted in specified food commodities. The levels of pesticide residues present in food are not permitted to exceed the MRLs/EMRLs

specified in Schedule 1. For pesticide residues with no specified MRLs/EMRLs in Schedule 1, the Regulation stipulates that except for exempted pesticides, import or sale of food containing such pesticide residues is allowed if the consumption of the food concerned is not dangerous or prejudicial to health based on risk assessment conducted by the Centre for Food Safety (CFS).[24]

35. According to the regulation, MXC is not listed in the Schedule 1 and is not listed as an exempted pesticide. As such, CFS will conduct risk assessment on the detected level of MXC in a food sample based on local food consumption pattern and the available safety reference values, to protect public health in Hong Kong.[24]

Scope of Study

36. To estimate the dietary exposure to MXC of the Hong Kong adult population, this study analysed the levels of MXC in selected food items which were chosen mainly based on their popularity among the local adult population, their MXC levels reported in the literature, and their availability in the local market during the sampling period. These samples were classified into 14 different food groups, including “Cereals and grains products”, “Vegetables”, “Fruits”, “Nuts and seeds”, “Meats and offals”, “Eggs and egg products”, “Milk and dairy products”, “Fishes”, “Fish products”, “Crustaceans and molluscs”, “Fats and oils”, “Beverages”, “Herbs and spices” and “Honey”.

Methodology and Laboratory Analysis

Methodology

37. Food samples were collected between July and December 2022 from various retail outlets such as wet markets, online shopping platform, physical supermarkets and grocery stores, etc. The food items analysed are listed in **Appendix**. Only the edible portions of the samples were analysed, and all samples were prepared in the form of food "as consumed" before chemical analysis. The analytical results were then combined with the food consumption information from the Hong Kong Second Population-based Food Consumption Survey 2018-2020 to obtain the dietary exposures of local adult population.[25]

38. The estimation of dietary exposures was performed with the aid of an in-house developed web-based computer system, Exposure Assessment System (EASY). The mean and 90th percentile exposure levels were used to represent the dietary exposure levels of average and high consumers of the local population, respectively.

Laboratory Analysis

39. Laboratory analysis of MXC was conducted by the Food Research Laboratory (FRL) of CFS.

40. Levels of MXC in food samples were analysed by gas chromatography - tandem mass spectrometry (GC-MS/MS). Stable isotope labelled MXC was spiked quantitatively into a measured amount of sample. Sample extraction was carried out by vertical shaking with a mixture of water, acetonitrile and formic acid. A buffer salt mixture was

added for salting out the organic acetonitrile level. The organic extract was purified by dispersive solid phase extraction (SPE). After sample purification, the sample solution was concentrated in iso-octane and subjected to instrumental analysis. The limit of detection (LOD) of MXC was 0.1 µg/kg.

Treatment of Analytical Values Below the LOD

41. In this study, analytical results were treated by the lower-bound (LB) and upper-bound (UB) approach, i.e. results below the LOD were assigned a value of zero or the value of LOD for the LB and UB, respectively. This approach compares the two extreme scenarios, based on the consideration that the true value for results smaller than LOD may actually be any value between zero and the LOD. The LB scenario assumes the chemical is absent whilst the UB scenario assumes that the chemical is present at the level of the LOD. The medium-bound (MB) level of MXC amount in food is also calculated, by assigning results below LOD as one half the LOD.[26]

Results and Discussion

Occurrence of MXC

42. Of the 300 samples analysed, all samples were not detected with MXC. In the chemical testing of this study, the LOD for MXC was 0.1 µg/kg.

43. For MXC in all samples, the LB mean concentrations were 0 µg/kg, the MB mean concentrations were 0.05 µg/kg and the UB mean concentrations were 0.1 µg/kg. The mean MXC concentrations of food samples are shown in **Appendix**.

44. The mean MXC concentrations in different groups were calculated by dividing the total MXC concentration of all samples in the same group by the number of samples in the group. Assuming all samples contained the highest possible level of MXC, i.e. 0.1 µg/kg, the mean MXC concentrations in different groups were 0.1 µg/kg.

Dietary Exposure to MXC

45. Regarding the dietary exposure to MXC of the local adult population, the LB and UB exposure estimates of MXC for average consumers are 0 and 0.002283 µg/kg bw/day respectively, while for high consumers (90th percentile), the LB and UB exposure estimates are 0 and 0.003608 µg/kg bw/day respectively. These dietary exposures are much lower than the JMPR ADI of 100 µg/kg bw/day, indicating that the adverse health effects for average and high consumers of the population due to MXC upon usual consumption of food are unlikely.

Major Food Contributor

46. Since the results for all samples were below the LOD, the actual food group contribution to the overall MXC exposure was not reflected.

Uncertainties and Limitations of the Study

47. While higher accuracy and precision in exposure estimation could be achieved with more samples analysed, compromises had to be made in relation to the use of finite resources. In this study, only selected food items

that were commonly consumed and reported more likely to contain MXC were sampled. Furthermore, the results of this study could only represent a snapshot of MXC levels in certain locally available foods.

Conclusions and Recommendations

48. In this study, all 300 samples were not detected with MXC, with the LOD of 0.1 μg/kg. The estimated dietary exposures to MXC for the Hong Kong adult population indicate that the current dietary exposure to MXC for the Hong Kong adult population does not raise a health concern.

49. In Hong Kong, the Pesticide Residues including MXC residues in food is regulated by the Pesticide Residues in Food Regulation (Cap. 132CM). For pesticide residues with no specified MRLs/EMRLs in Schedule 1 in the Regulation, the Regulation stipulates that except for exempted pesticides, import or sale of food containing such pesticide residues is allowed if the consumption of the food concerned is not dangerous or prejudicial to health based on risk assessment conducted by CFS. CFS has been closely monitoring the latest international development of regulatory control and will review the regulatory standard, as necessary and appropriate.

50. The findings of the dietary exposures to MXC in the present study did not provide sufficient justifications to warrant changes to the basic dietary advice on healthy eating. The public is advised to maintain a balanced and varied diet which includes a wide variety of fruit and vegetables so as to avoid excessive exposure to any contaminants from a small range of food items.

Reference

[1] United Nations. Stockholm Convention on Persistent Organic Pollutants. Report of the Persistent Organic Pollutants Review Committee on the work of its sixteenth meeting: Risk profile for methoxychlor. UNEP/POPS/POPRC.16/9/Add.1. 2021. http://chm.pops.int/TheConvention/POPsReviewCommittee/Meetings/POPRC16/Overview/tabid/8472/Default.aspx

[2] Insecticide Resistance Action Committee. The IRAC Mode of Action Classification Online. Accessed on 30 March 2023. https://irac-online.org/mode-of-action/classification-online

[3] Blum JL, Nyagode BA, James MO, Denslow ND. Effects of the pesticide methoxychlor on gene expression in the liver and testes of the male largemouth bass (Micropterus salmoides). Aquat Toxicol. 2008 Mar; 86(4):459-69. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3004021/pdf/nihms243579.pdf

[4] U.S. Department of Health and Human Services, Public Health Service. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Methoxychlor. 2002. https://www.atsdr.cdc.gov/ToxProfiles/tp47.pdf

[5] U.S. Environmental Protection Agency (EPA). Methoxychlor Reregistration Eligibility Decision (RED). EPA 738-R-04-010. 2004. https://archive.epa.gov/pesticides/reregistration/web/html/methoxychlor_red.html

[6] United Nations Environmental Programme. Stockholm Convention. Invitation for information and comments following the decisions taken by the Persistent Organic Pollutants Review Committee at its sixteenth meeting (POPRC-16). 2021. http://chm.pops.int/TheConvention/POPsReviewCommittee/Meetings/POPRC16/POPRC16Followup/tabid/8748/Default.aspx

[7] World Health Organization. Methoxychlor in Drinking-water: Background document for development of WHO Guidelines for Drinking-water Quality. WHO/SDE/WSH/03.04/105. 2004. https://cdn.who.int/media/docs/default-source/wash-documents/wash-chemicals/methoxychlor.pdf?sfvrsn=10e4ad65_4

[8] European Food Safety Authority (EFSA), Medina-Pastor P, Triacchini G. The 2018 European Union report on pesticide residues in food. EFSA Journal. 2020 Feb;18(4):6057. https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2020.6057

[9] Bolor VK, Boadi NO, Borquaye LS and Afful S. Human risk assessment of organochlorine pesticide residues in vegetables from Kumasi, Ghana. Hindawi, Journal of Chemistry, 2018 May. Article ID 3269065. https://downloads.hindawi.com/journals/jchem/2018/3269065.pdf

[10] Adeleye AO, Sosan MB, Oyekunle JAO. Occurrence and Human Health Risk of Dichlorodiphenyltrichloroethane (DDT) and Hexachlorocyclohexane (HCH) Pesticide Residues in Commonly Consumed Vegetables in Southwestern Nigeria. J. Health Pollut. 2019 Sept;9(23):190909. https://meridian.allenpress.com/jhp/article/9/23/190909/445463/Occurrence-and-Human-Health-Risk-of

[11] Food and Agriculture Organization of the United Nations/ World Health Organization. Evaluation of the toxicity of pesticide residues in Food. Methoxychlor. 1965. https://inchem.org/documents/jmpr/jmpmono/v065pr31.htm

[12] Food and Agriculture Organization of the United Nations, World Health Organization. Pesticide residues in Food. Methoxychlor. 1977. https://inchem.org/documents/jmpr/jmpmono/v077pr37.htm

[13] U.S. Environmental Protection Agency. Methoxychlor. 72-43-5. 2000. https://www.epa.gov/sites/default/files/2016-09/documents/methoxychlor.pdf

[14] World Health Organisation, International Agency for research on cancer (IARC). IARC monographs on the evaluation of the carcinogenic risks to humans. Overall Evaluations of Carcinogenicity: An Updating of IARC Monographs volumes 1 to 42. Supplement No. 7. 1987. https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-Supplements/Overall-Evaluations-Of-Carcinogenicity-An-Updating-Of-IARC-Monographs-Volumes-1%E2%80%9342-1987

[15] Chen G. Methoxychlor. Reference Module in Biomedical Sciences. Encyclopedia of Toxicology (Third edition), 2014 Apr; Pages 254-5. https://www.sciencedirect.com/science/article/pii/B9780123864543001627?via%3Dihub

[16] Golub MS, Hogrefe CE, Germann SL, Lasley BL, Natarajan K and Tarantal AF. Effects of Exogenous Estrogenic Agents on Pubertal Growth and Reproductive System Maturation in Female Rhesus Monkeys. Toxicol Sci. 2003 July;74(1): 103-13. https://www.semanticscholar.org/paper/Effects-of-exogenous-estrogenic-agents-on-pubertal-Golub-Hogrefe/a7deb64482d2e79d90b7ab3f7aae94750045e986

[17] Freire C, Koifman RJ, Sarcinelli PN, Simoes Rosa AC, Clapauch R, Koifman S. Long-term exposure to organochlorine pesticides and thyroid status in adults in a heavily contaminated area in Brazil. Environ Res. 2013 Nov;127:7-15.

[18] European Commission. EU Pesticides Database – MRLs. Methoxychlor. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/mrls/details?lg_code=EN&pest_res_id_list=158&product_id_list=

[19] U.S. Environmental Protection Agency. 40 CFR Part 180 Methoxychlor; Tolerance Revocations. Federal Register: July 17, 2002; 67(137): 46906-9. https://www.govinfo.gov/content/pkg/FR-2002-07-17/pdf/FR-2002-07-17.pdf

[20] Agricultural and Veterinary Chemicals Code (MRL Standard) Instrument 2019. https://www.legislation.gov.au/Details/F2021C00087

[21] Government of the People's Republic of China, National Health Commission, Ministry of Agricultural and Rural Affairs, State Adminstration of Market Regulation. National Food Safety Standard – Maximum Residue Limits for Pesticide in Food (GB 2763-2021). 2021 Mar; 178-9. http://www.chinapesticide.org.cn/oldfile/181729272s82.pdf

[22] United Nations. Stockholm Convention on Persistent Organic Pollutants. Decision: Methoxychlor. POPRC-17/1. Feb 2022. http://chm.pops.int/TheConvention/POPsReviewCommittee/Meetings/POPRC17/Overview/tabid/8900/Default.aspx

[23] The Government of the Hong Kong Special Administrative Region Agriculture, Fisheries and Conservation Department. Pesticides. Pesticide Control and Related Information. https://www.afcd.gov.hk/english/quarantine/qua_pesticide/qua_pes_pes/qua_pes_pes_prc.html

[24] The Government of the Hong Kong Special Administrative Region. Food and Environmental Hygiene Department. Food Legislation/ Guidelines. Pesticide Residues in Food Regulation. https://www.cfs.gov.hk/english/whatsnew/whatsnew_fstr/whatsnew_fstr_21_Pesticide.html

[25] The Government of the Hong Kong Special Administrative Region. Food and Environmental Hygiene Department. Centre for Food Safety. Report of the Second Hong Kong Population-Based Food Consumption Survey. 2021 June.
https://www.cfs.gov.hk/english/programme/programme_firm/files/2nd_FCS_Report_29_Jun_2021.pdf

[26] World Health Organization (WHO). Environmental Health Criteria 240. Principles and Methods for the Risk Assessment of Chemicals in Food. Chapter 6: Dietary Exposure Assessment for Chemicals in Food. 6.5.4 Handling results below the LOD or LOQ.
https://inchem.org/documents/ehc/ehc/ehc240_chapter6.pdf

Mean Levels of Methoxychlor (µg/kg) Detected in Food Samples

Food Item	No. of samples	Mean of MXC (µg/kg)		
		Lower-bound	Medium-bound	Upper-bound
Food Group 1: Cereals and Grains Products	**27**	**0**	**0.05**	**0.1**
(1) White rice	3	0	0.05	0.1
(2) Instant noodles	3	0	0.05	0.1
(3) Macaroni	3	0	0.05	0.1
(4) Spaghetti	3	0	0.05	0.1
(5) Udon	3	0	0.05	0.1
(6) Oatmeal	3	0	0.05	0.1
(7) Wheat bread	3	0	0.05	0.1
(8) White bread	3	0	0.05	0.1
(9) Saltine crackers	3	0	0.05	0.1
Food Group 2: Vegetables	**66**	**0**	**0.05**	**0.1**
(1) Red radish/Carrot	3	0	0.05	0.1
(2) Potato	3	0	0.05	0.1
(3) Chinese flowering cabbage	3	0	0.05	0.1
(4) Chinese lettuce	3	0	0.05	0.1
(5) Iceberg lettuce	3	0	0.05	0.1
(6) Pak-choi	3	0	0.05	0.1
(7) Celery	3	0	0.05	0.1
(8) Broccoli	3	0	0.05	0.1
(9) European variety cabbage	3	0	0.05	0.1
(10) Hairy gourd	3	0	0.05	0.1
(11) Pumpkin	3	0	0.05	0.1
(12) Corn kernel	3	0	0.05	0.1
(13) Chili pepper	3	0	0.05	0.1
(14) Sweet pepper	3	0	0.05	0.1
(15) Tomato	3	0	0.05	0.1
(16) Onion	3	0	0.05	0.1
(17) Green string beans (with pod)	3	0	0.05	0.1
(18) Red bean	3	0	0.05	0.1
(19) Black-eyed pea	3	0	0.05	0.1
(20) Tofu	3	0	0.05	0.1
(21) Button mushroom	3	0	0.05	0.1
(22) Winter mushroom (dry)	3	0	0.05	0.1

Food Item	No. of samples	Mean of MXC (μg/kg)		
		Lower-bound	Medium-bound	Upper-bound
Food Group 3: Fruits	**42**	**0**	**0.05**	**0.1**
(1) Apple	3	0	0.05	0.1
(2) Pear	3	0	0.05	0.1
(3) Guava	3	0	0.05	0.1
(4) Cantaloupe	3	0	0.05	0.1
(5) Mandarin	3	0	0.05	0.1
(6) Orange	3	0	0.05	0.1
(7) Grape	3	0	0.05	0.1
(8) Banana	3	0	0.05	0.1
(9) Dragon fruit	3	0	0.05	0.1
(10) Kiwifruit	3	0	0.05	0.1
(11) Mango	3	0	0.05	0.1
(12) Papaya	3	0	0.05	0.1
(13) Pineapple	3	0	0.05	0.1
(14) Watermelon	3	0	0.05	0.1
Food Group 4: Nuts and Seeds	**15**	**0**	**0.05**	**0.1**
(1) Almond	3	0	0.05	0.1
(2) Cashew nut	3	0	0.05	0.1
(3) Walnut	3	0	0.05	0.1
(4) Peanut	3	0	0.05	0.1
(5) Coconut milk	3	0	0.05	0.1
Food Group 5: Meat and Offal	**24**	**0**	**0.05**	**0.1**
(1) Beef	3	0	0.05	0.1
(2) Pork	3	0	0.05	0.1
(3) Lamb	3	0	0.05	0.1
(4) Pig large intestine	3	0	0.05	0.1
(5) Pig liver	3	0	0.05	0.1
(6) Pig stomach	3	0	0.05	0.1
(7) Chicken meat	3	0	0.05	0.1
(8) Duck meat	3	0	0.05	0.1
Food Group 6: Egg and Egg Products	**9**	**0**	**0.05**	**0.1**
(1) Chicken egg	3	0	0.05	0.1
(2) Lime preserved egg	3	0	0.05	0.1
(3) Salted duck egg	3	0	0.05	0.1
Food Group 7: Milk and Dairy Products	**15**	**0**	**0.05**	**0.1**
(1) Skimmed milk	3	0	0.05	0.1
(2) Whole milk	3	0	0.05	0.1
(3) Whipping cream	3	0	0.05	0.1
(4) Cheese	3	0	0.05	0.1
(5) Yoghurt	3	0	0.05	0.1

Food Item	No. of samples	Mean of MXC (μg/kg)		
		Lower-bound	Medium-bound	Upper-bound
Food Group 8: fish	**30**	**0**	**0.05**	**0.1**
(1) Bighead carp	3	0	0.05	0.1
(2) Freshwater grouper	3	0	0.05	0.1
(3) Goldfish carp	3	0	0.05	0.1
(4) Grass carp	3	0	0.05	0.1
(5) Mud carp	3	0	0.05	0.1
(6) Golden thread	3	0	0.05	0.1
(7) Pomfret	3	0	0.05	0.1
(8) Yellow croaker	3	0	0.05	0.1
(9) Salmon	3	0	0.05	0.1
(10) Thread fish	3	0	0.05	0.1
Food Group 9: Fish products	**12**	**0**	**0.05**	**0.1**
(1) Canned dace	3	0	0.05	0.1
(2) Canned tuna	3	0	0.05	0.1
(3) Fish ball/fish cake	3	0	0.05	0.1
(4) Fish siu mai	3	0	0.05	0.1
Food Group 10: Crustaceans and Molluscs	**18**	**0**	**0.05**	**0.1**
(1) Shrimp/prawn	3	0	0.05	0.1
(2) Crab	3	0	0.05	0.1
(3) Abalone	3	0	0.05	0.1
(4) Clam	3	0	0.05	0.1
(5) Scallop	3	0	0.05	0.1
(6) Squid	3	0	0.05	0.1
Food Group 11: Fats and Oils	**18**	**0**	**0.05**	**0.1**
(1) Butter	3	0	0.05	0.1
(2) Canola oil	3	0	0.05	0.1
(3) Corn oil	3	0	0.05	0.1
(4) Margarine	3	0	0.05	0.1
(5) Olive oil	3	0	0.05	0.1
(6) Peanut oil	3	0	0.05	0.1
Food Group 12: Beverages	**9**	**0**	**0.05**	**0.1**
(1) Coffee	3	0	0.05	0.1
(2) Bottled tea	3	0	0.05	0.1
(3) Bottled water	3	0	0.05	0.1
Food Group 13: Herbs and Spices	**12**	**0**	**0.05**	**0.1**
(1) Chinese parsley	3	0	0.05	0.1
(2) Lemon grass	3	0	0.05	0.1
(3) Curry powder	3	0	0.05	0.1
(4) Ginger	3	0	0.05	0.1
Food Group 14: Honey	**3**	**0**	**0.05**	**0.1**
(1) Honey	3	0	0.05	0.1

* The mean levels of MXC amount in all samples are below LOD, which are assigned a value of zero or the value of LOD for the lower-bound (LB) level and upper-bound (UB) level of MXC amount in food, respectively. The medium-bound (MB) level of MXC amount in food is also calculated, by assigning results below LOD as one half the LOD.