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Chemistry 3010 Research Project

Chemical: Difenoconazole

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Abstract

An environmental risk assessment was conducted to assess the potential environmental and physical risks of Difenoconazole, a widely used triazole fungicide that is registered in Canada. This chemical compound was detected in a single unfiltered sample of Lake Okanagan, a region renowned for its productive fruit orchards and crops. Due to unprecedented heavy rains this Fall, it is presumed the chemical was used, according to regulations, as a pesticide in adjacent orchards and crops and reached the lake via groundwater or run-off. A thorough literature review yielded valuable information regarding relevant properties of the chemical compound to assist in the assessment. Characteristics of note include a large organic carbon/water partition coefficient (K_{oc}), suggesting Difenoconazole rapidly partitions into the organic matter within the sediment or suspended matter of a lake rather than air surrounding or water within the environment. Further, the chemical was deemed very toxic to aquatic life, however only moderately toxic to human life. An analysis of the literature concluded Difenoconazole does not pose a significant threat towards the ecosystem or human usage of Lake Okanagan, however continued analysis of the lake for the chemical should be conducted to ensure the aquatic organisms are not detrimentally impacted.

Table of Contents

Introduction

This Fall Difenoconazole was detected in an unfiltered water sample of Okanagan Lake, a lake which is used for irrigation, domestic consumption, and recreation. Difenoconazole is a chemical compound globally used in agriculture as a pesticide to protect crops from fungal diseases. The region surrounding Okanagan Lake is considered as one of the warmest in Canada, leading the land to be abundant with fruit orchards and crops. As Difenoconazole is a commonly used Fungicide in British Columbia, it is likely a fruit orchard or crop adjacent to the Okanagan Lake was sprayed or had Difenoconazole used as a seed treatment.[12] The sample was collected within 500 meters of the shoreline and approximately 2 meters deep. As well, the sample was unfiltered and as such contained suspended particulate within the aqueous solution. As this lake is multi-purposeful, concerns were quickly raised an in-depth literature review was deemed necessary to evaluate potential environmental and physical risks of this compound.

I. Difenoconazole

The chemical being investigated in this report is Difenoconazole. It is a 1,3-dioxolane and has a chemical formula of $C_{19}H_{17}Cl_2N_3O_3$, with the chemical structure represented in Figure. 1. Possible degradation products of Difenoconazole were found and termed TP295, TP295A, TP354A, TP387A and CGA205375.[3] Physical properties of Difenoconazole are shown in Table.1 and environmental partition coefficients are outlined in Table. 2.

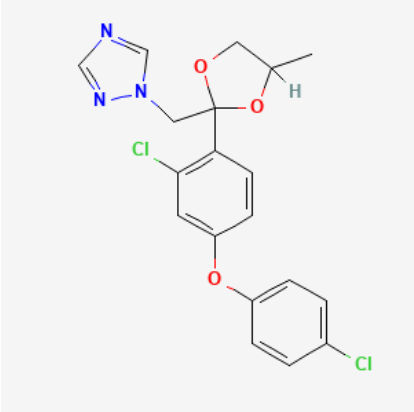

Figure. 1 Chemical structure of Difenoconazole[1]

Table. 1 Physical Properties of the Chemical Difenoconazole.

Molecular Weight [1]	406.3 g/mol
Color/Form [1]	White Crystalline Solid
Odor [1]	Odorless
Boiling Point [1]	100.8 ℃
Melting Point [1]	76 ℃
Vapour Pressure at 25 ℃ [2]	3.3 x 10^{-5} mPa (2)
Solubility in Water [2]	15 mg/L

Table. 2 Environmental Partition Coefficients of Difenoconazole

N-Octanol/Water Partition Coefficient at 25 ℃ [2]	log K_{ow} = 4.4
Henry's Law Constant (H) [2]	8.22 x 10^{-12} atm x m^3/mol
Air/Water Partition Coefficient at 25 ℃ (K_{aw}) *	3.31 x 10^{-15}
Organic Carbon-Water Partition Coefficient (K_{oc}) [2]	2237-11034
Bioconcentration Factor (BAF) [2]	570

* calculated for 25 ℃ from Henry's Law Constant

II. Uses, Sources and Route of Entry to Environment and Lake

Difenoconazole is used as a broad-spectrum fungicide that is used as either a spray or seed treatment to control diseases on field crops, including fruits, vegetables, and cereals.[1,4] Diseases this chemical protects from include powdery mildew, black rot, Phomopsis cane and leaf spot.[15] This chemical is exposed to the environment after being sprayed or spread over crops which can cause it to leach into the soil and reach the lake through run-off or groundwater. Possible degradation products that can be found in the environment were reported by Yanli Man et al. with the transformation reactions being oxidation, dechlorination and hydroxylation, all of which are naturally occurring.[3]

III. Registration in Canada

Difenoconazole is currently registered under the *Pest Control Products Act* in Canada as of March 2016.[2] However, Health Canada is consulting with Canadian's on whether to continue Difenoconazole's registration in Canada as of May 28th, 2021. As of November 11th, 2021, no decision on the continued registration of Difenoconazole has been made.[5] Applicable regulations of Difenoconazole, such as buffer regions, are specific to the method of application with the largest being 30 m between the point of direct application and a freshwater habitat.[2]

Figure. 2 Example application of Fungicide to a crop.[16]

IV. Potential Impacts on Lake Water Quality and Environment

Due to the high K_{oc} value, Difenoconazole partitions into the organic matter of soil, sediment or suspended matter as seen in aquatic environments. Although an accumulation of Difenoconazole can pose be hazardous at high concentrations it is unlikely to reach these concentrations through its intended use. Research conducted by Bruno Keni Ortic Canavate et al. suggested that at environmentally relevant concentrations fungicides have the potential to interfere with the ecosystem by inhibiting cyanobacterial natural competitors, such as parasitic fungi, which causes the promotion of harmful algal blooms.[13] These blooms can potentially affect the water quality of Lake Okanagan and have a toxic effect towards the ecosystem of the lake. If left unchecked, such algal blooms could accelerate the rate of trophication of Okanagan Lake and indirectly affect the water quality in a detrimental fashion. Relatively little research is conducted on fungicides relative to herbicides and insecticides, however it is noted by Zachary R. Stanley that fungicides have been found to be harmful to ciliate protozoa.[14] This group of protists are prevalent in most waters and aid in the removal of bacteria and protozoa in the environment. Therefore, these organisms can be

affected with the detection of Difenoconazole in Lake Okanagan. Although, it should be noted Health Canada deemed the environmental risk of Difenoconazole to be acceptable under the current conditions of use.[2]

V. Where Difenoconazole is Distributed or Stored in the Environment

Once in the environment, Difenoconazole is distributed largely by rainfall both horizontally and vertically.[8] A study conducted by Fangfang Zhao et al. suggested that Difenoconazole can be found in both the shallow and deep layers of the soil.[7] As the reported organic carbon/water partition coefficient (K_{oc}) value is large, 2237-11034, it can be inferred that Difenoconazole prefers partitioning to the organic carbon in soil or sediment rather than the water. The high K_{oc} value indicates Difenoconazole has slight mobility to immobility in soil as well as mild persistence in aerobic soil and persistence in anaerobic soil.[2,9] Further, in an aquatic environment, such as a lake, Difenoconazole partitions rapidly into the organic matter within the sediment and is largely hydrophobic due to the high K_{oc} value. This further indicates Difenoconazole has the potential to sorb onto suspended organic particulate found in water bodies. Additionally, as evidenced by the small air/water partition coefficient (K_{aw}) it can be inferred Difenoconazole prefers the water rather than the air. This proposes that the concentration of Difenoconazole in the atmosphere above the lake and orchard/crop is insignificant. The high octanol-water partition coefficient (K_{ow}) suggested Difenoconazole has the potential to bioaccumulate and a study by Lemeng Zhang et al. demonstrated this property by finding Difenoconazole to bioaccumulate in the muscles of marine medaka.[2,8]

VI. Potential Hazard or Adverse Effects of Difenoconazole

The Globally Harmonized System of Classification and Labelling of Chemicals (GHS) hazard statement outlines that Difenoconazole is both acutely and chronically toxic to aquatic life.[1] Research by Xiyan Mu et al. in 2016 used Zebrafish to study the toxicity of this chemical on aquatic organisms, as it is considered a model vertebrate organism.[10] This study concluded that Difenoconazole causes hatching inhibition, abnormal spontaneous movement, slow heart rate, growth regression and morphological deformities. Transformation products of Difenoconazole were also found to be toxic to amphibians, freshwater and marine/estuarine invertebrates and fish as well as freshwater algea.[1] Further, as explained in Section V., aquatic organisms are threatened due to the high bioaccumulation potential of Difenoconazole as concluded by Lemeng Zhang et al.[8]

Conversely, Difenoconazole was found to have low acute toxicity when test mammals ingested, inhaled, or were exposed to Difenoconazole on the dermal layer.[11] The health effects found in animals occurred at doses more than 100-times higher than levels to which humans are normally exposed if used in accordance to the regulations.[2] Further, chronic dietary intake estimates indicated that the general population is only exposed to 12 % to 30 % of the acceptable daily intake, being 0.1 mg/kg bw/day as stated by the Health Canada.[2] Relevant No Observed Adverse Effect Levels (NOAEL's) from the European Safety Authority can be found in Table. 3.[9] These values suggest that the doses at which no adverse effects occur are larger for short periods and substantially smaller for long durations of time. Acute reference doses' (ARfD's) were calculated by Health Canada and was determined to be 0.08 mg/kg bw for females (13-49 years of age) and 0.3 mg/kg bw for the general

population excluding females of 13-49 years of age.[2] Lastly, Difenoconazole was found to be unlikely to be a carcinogen and genotoxic *in vivo* to humans.[9]

Table. 3 Relevant No Observed Adverse Effect Levels (NOAEL's) concluded by the European Food Safety Authority.[9]

Short term NOAEL in the rat (90-day study)	20 mg/kg bw/day
Long term NOAEL in the rat	1.0 mg/kg bw/day
Short term NOAEL in the mouse (90-day study)	34 mg/kg bw/day
Long term NOAEL in the mouse	4.7 mg/kg bw/day
Short term NOAEL in the dog (28 week study)	31 mg/kg bw/day

VII. Assessment of Situation

Difenoconazole was found in an unfiltered water sample of Lake Okanagan, a lake within a region well known for its wineries and fruit orchards. As Difenoconazole is a commonly used pesticide for fruits, among other plants, it is sensible that an adjacent orchard or crop was sprayed or had Difenoconazole used as a seed treatment whilst following applicable regulations. With the unprecedented heavy rains this Fall, this chemical reached the lake in elevated concentrations by way of run-off or groundwater. Once in the environment Difenoconazole has the possibility to transform into other products through oxidation, dechlorination and hydroxylation.[3] With an assessment of Difenoconazole's partition coefficients, this compound prefers the organic matter within soil or sediment rather than air or water and is slightly mobile to immobile once in soil or sediment. This suggests that as Difenoconazole was being distributed to the lake, a large concentration stayed in soil rather than reach the lake water. Further indicating the concentration of Difenoconazole which reached the lake is small and therefore does not detrimentally affect the water quality. Further, as the sample was not filtered it is possible the detected Difenoconazole was adsorbed to the particulate in the sample. The environmental persistence of Difenoconazole

is concerning, although Health Canada concluded the environmental risk is acceptable under the current conditions of use.[2] However, this chemical does have a slight penchant to bioaccumulate in aquatic organisms.[2] As well, multiple reports indicated the high toxicity of Difenoconazole on aquatic organisms, although a low toxicity for mammals, such as rats or mice, was found. Health Canada reported the acceptable daily intake of 0.1 mg//kg bw/day for humans, however it was found that hazardous health effects in animals occur at 100 times higher than the average exposure.[2] Altogether, due to the heavy rains this spring Difenoconazole could be detected in Okanagan Lake in unprecedented concentrations. Although this chemical does not pose a significant threat on the health of the environment as well as humans, it is highly toxic towards aquatic life and future levels of the compound should be monitored.

Conclusion

Difenoconazole, a registered pesticide in Canada, was detected in a single unfiltered water sample in Lake Okanagan this fall. Due to the heavy rains, it is likely this chemical compound made its way to the lake via run-off or groundwater. Since the sample was unfiltered, the Difenoconazole was likely detected on the suspended particulate as environmental partition coefficients, namely the high octanol/water partition coefficient, indicate the chemical readily adsorbs to the organic matter in the lake sediment rather than water or air. An extensive literary review concluded Difenoconazole poses minimal risk to humans and animals who utilize the multipurposed Lake Okanagan. However, due to the high toxicity of Difenoconazole towards aquatic life, it is recommended samples of Lake Okanagan should be analyzed every 2 months to ensure the chemical does not rapidly increase in concentration.

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