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RISK ASSESSMENT OF CYCLODODEC-2-EN-1-YL ETHERS IN THE ENVIRONMENT

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ABSTRACT

Environmental pollutants are continuously being emitted from anthropogenic activities in large amounts. They move throughout the ecosystem by a variety of processes and are eventually degraded or accumulated somewhere in the environment. The chemical diversity of pollutants and the variations in behaviour, both with respect to transport, degradation, accumulation (fate) and toxicity (effects) has introduced the field of risk assessment. It needs to be based on an interdisciplinary approach involving monitoring of exposure concentrations in the natural environment, laboratory scale fate and effect studies and predictive models designed to establish a quantitative link between sources, exposure levels, and risk of effects of potential hazardous pollutants. The aim of this work is to predict risk assessment of some new synthesized chemicals (cyclododec-2-en-1-yl ethers) in the environment.

Key words: *Risk assessment, persistence, bioaccumulation, toxicity, cyclododec-2-en-1-yl ethers*

INTRODUCTION

New chemicals are continuously being introduced to the environment either directly (primary emission) or indirectly as an unintended result of the use. The pollution caused by synthetic organic chemicals has brought about severe lessons to human beings. Persistent toxic substances (PTS) in the environment have become an important issue affecting the survival and development of human in the 21st century [1].

Environmental risk assessment (ERA) involves evaluating the potential for persistence, accumulation and toxicity of chemicals in the environment in order to manage these risks to protect the environment and the organisms living in it [2]. One major group of organic substances of concern is called PBTs (Persistent, Bioaccumulative, Toxic substances). PBTs are persistent because they remain unchanged for a relatively long time in the environment. Moreover, these chemicals are not easily metabolized or excreted and therefore tend to accumulate in organisms [3]. These chemicals also hold toxic properties and hence are harmful to wildlife and the ecosystem [4].

Scientific and regulatory activity in environmental (ecological) risk assessment continues to progress globally. In Europe, the REACH programme, together with new requirements for the ERA of human pharmaceuticals, represent significant developments in regulatory ERA procedures for industry. The Organisation for Economic Co-operation and Development (OECD), for example, has been developing in vitro and in vivo mammalian and wildlife test guidelines for assessing the developmental and reproductive effects of chemicals in the environment [5, 6].

It is evident that ecological risk assessment (ERA) for the synthetic organic compounds can provide a precaution against the pollution [1]. ERA includes three primary phases as defined by U.S. Environmental Protection Agency (US EPA): problem formulation, analysis, and risk characterization [7]. It is obvious that data on physicochemical properties, environmental behavior and ecotoxicology of organic compounds, are indispensable for the ERA. However, the data have three aspects of problems: 1) Lack of the data [8]; 2) Large expense of testing [9]; 3) Uncertainty in data [10].

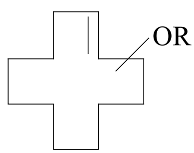
Molecular structures are internal factors governing the physicochemical properties, environmental behaviour and ecotoxicology of organic compounds. Compounds with similar molecular structures should have similar physicochemical properties, environmental fate and ecotoxicological effects, i.e., there are inherent relations between molecular structures and their physicochemical properties, environmental behavioral and ecotoxicological parameters [11]. Thus, (Q) SARs can fill the data gap for physicochemical, environmental behavioral and ecotoxicological parameters of organic compounds; they also can decrease experimental expenses and reduce the extent of experimental testing (especially animal testing). Furthermore, (Q)SARs can be used as supporting tools to evaluate the adequacy of the available empirical data of organic compounds, which is also one of the four specific functions of (Q)SARs for ERA [12]. Thus (Q)SAR technology is of great importance to ERA of organic compounds [13].

Among the numerous compounds used in perfume industry nowadays, methoxy – and ethoxycyclododecanes as well as (2-methoxyethoxy) – and (2-ethoxyethoxy) cyclododecanes hold an important position. The commonly accepted procedures for the preparation of these compounds are multi-stage, and some of the reaction steps are associated with the formation of highly-toxic, explosive, or expensive chemicals. The cyclododec-2-en-1-yl ethers are derived by the catalytic substitution reaction between isomeric cyclododec-2-en-1-yl acetates [14] and primary aliphatic alcohols in the presence of $Pd^0[PPh_3]_4$ [15]. The new synthesized chemicals as the cyclododec-2-en-1-yl ethers can be introduced to the environment which need to be explored the environmental risk assessment of these compounds.

The aim of this work is to predict the potential for persistence, bioaccumulation and toxicity of some new synthesized chemicals (cyclododec-2-en-1-yl ethers) in the environment.

MATERIALS AND METHODS

Compound Data. Some new synthesized chemicals (cyclododec-2-en-1-yl ethers) are presented in Tables 1 [15].



R represents: CH_3, C_2H_5, $C_2H_4OCH_3$ or $C_2H_4OC_2H_5$

Criteria used by the PBT Profiler. The PBT Profiler is a screening-level tool that provides estimates of the persistence, bioaccumulation, and chronic fish toxicity potential of chemical compounds. It is designed to be used when data are not available. In order to help interested parties make informed decision on a chemical's PBT characteristics, the PBT profiler automatically identifies chemicals that may persistent in the environment and bioaccumulate in the food chain. These chemicals are identified using thresholds published by the Environmental Protection Agency (EPA) [16].

Persistence criteria. The PBT Profiler combines the persistence criteria for water, soil, and sediment and highlights chemicals with an estimated half-life ≥ 2 months and < 6 months as persistent and those with an estimated half-life ≥ 6 months as very persistent. The half-life in air is not used in the PBT Profiler's Persistence summary (chemicals with an estimated half-life > 2 days are considered as persistent). The PBT Profiler uses 30 days in a month for its comparisons.

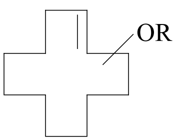
Bioaccumulation criteria. The PBT Profiler combines the bioaccumulation criteria and highlights chemicals with a BCF (bioconcentration factor) ≥ 1000 and < 5000 as bioaccumulative and those with a BCF ≥ 5000 as very bioaccumulative.

Toxicity criteria. To highlight a chemical that may be chronically toxic to fish, the PBT profiler uses the following criteria: Fish ChV (Chronic Value) > 10 mg/l (low concern), Fish ChV = 0.1 – 10 mg/l (moderate concern) and Fish ChV < 0.1 mg/l (high concern).

RESULTS AND DISCUSSION

The results of the estimation of cyclododec-2-en-1-yl ethers for persistence, bioaccumulation and toxicity are presented in Table 1.

Table 1. *PBT Profiler Estimate of Cyclododec-2-en-1-yl Ethers*

№	Cyclododec-2-en-1-yl ethers 	Persistence		Bioaccumulation	Toxicity
		Media (water, soil, sediment, air) Half-life (days)	Percent in Each Medium	BCF	Fish ChV (mg/l)
1	R= – CH_3	15; 30; 140; 0.046	13%; 70%; 17%; 0%	1,000	0.003
2	R= – C_2H_5	38; 75; 340; 0.042	5%; 58%; 37%; 0%	2,200	0.0017
3	R= – $C_2H_4OCH_3$	38; 75; 340; 0.042	11%; 74%; 15%; 0%	680	0.005
4	R= – $C_2H_4OC_2H_5$	38; 75; 340; 0.042	8%; 61%; 32%; 0%	1,400	0.003

The PBT profiler uses a well-defined set of procedures to predict the persistence, bioaccumulation, and toxicity of chemical compounds when experimental data are not available. The persistence, bioaccumulation, and fish chronic toxicity values estimated by the PBT profiler are automatically compared to criteria published by EPA.

Persistence is the ability of a chemical substance to remain in an environment in an unchanged form. The longer a chemical persists, the higher the potential for human or environmental exposure to it. The individual environmental media for which a chemical's persistence is usually measured or estimated are air, water, soil, and sediment.

The PBT Profiler expresses persistence in individual medium half-lives in air, water, soil, and sediment measured in days. These half-lives are for reactivity-based persistence only. The EPA has established a series of proposed thresholds for persistence based on the efforts of scientists, regulators, and other interested parties worldwide in helping to identify and regulate chemicals that may present the greatest health and environmental risks [16].

Cyclododec-2-en-1-yl ethers from Table 1 are expected to be found predominantly in soil and their persistence estimate is based on their transformation in this medium. Half-life of compound 1 in soil, 30 days, does not exceed the EPA criteria. Therefore, ether 1 is estimated not to be persistent in the environment. While half-life of compounds 2–4 in soil, 75 days, exceeds the EPA criteria of > or = 2 months (and < or = 6 months). Therefore, these ethers are estimated to be persistent in the environment.

Humans, domestic animals, and wildlife are more likely to be exposed to a chemical if it does not easily degrade or is dispersed widely in the environment. The structural characteristics that enable a chemical to persist in the environment can also help it to resist metabolic breakdown in people or wildlife.

Bioaccumulation is the process by which the chemical concentration in an aquatic organism achieves a level that exceeds that in the water, as a result of chemical uptake through all possible routes of exposure. Biomagnification refers to the concentration of a chemical to a level that exceeds that resulting from its diet. Bioaccumulation includes both biomagnification and bioconcentration. In general, chemicals that have the potential to bioconcentrate also have the potential to bioaccumulate [16].

Bioconcentration in fish can be readily measured in the laboratory and is frequently used to predict the importance of bioaccumulation, which is much more complicated to determine. The potential for bioconcentration in fish is expressed as its bioconcentration factor, or BCF. The prediction of BCF is based on a chemical's octanol/water partition coefficient and one or more chemical structure-based correction factors, if applicable [16].

The estimated bioconcentration factor (BCF) for compounds 1, 2 and 4 from Table 1, exceeds the EPA bioconcentration criteria (> or = 1,000). The PBT Profiler estimates that ethers have the potential to bioconcentrate in fish and aquatic organisms and are expected to bioaccumulate in the food chain because it exceeds the BCF criteria. While the estimated bioconcentration factor (BCF) for compound 3,680, does not exceed the EPA bioconcentration criteria. Therefore, the PBT Profiler estimates that ether 3 is not expected to bioaccumulate in the food chain because it does not exceed the BCF criteria.

PBT chemicals are those that persist in the environment, bioconcentrate in aquatic organisms, and may bioaccumulate in humans, birds, and wild mammals. Exposure to PBT chemicals will result in chronic exposures which, in turn, leads to chronic toxicity [16].

The PBT Profiler estimates that cyclododec-2-en-1-yl ethers are chronically toxic to fish (Table 1). It is important to note that ethers may also be toxic to other aquatic organisms. Some aquatic organisms, such as daphnids, may be more sensitive to both acute and chronic exposures to ethers. The four ether compounds are with high toxicity (Fish ChV < 0.1 mg/l), which can be explained by metabolic transformation. A possible mechanism of cyclododec-2-en-1-yl ethers is to act as proelectrophiles by monooxygenase activation, which can be converted to acceptors of Michael-type [17]. Michael-type addition provides a means of covalent adduct formation at an electrophilic center, without any leaving group.

Chemicals can have a variety of toxic properties, resulting in a diverse array of adverse health effects. According to the EPA, the toxicity rating of a potential PBT chemical is based on repeated exposures which result in human or environmental toxicity. Adverse impacts can include mutagenic damage to DNA, cancer, neurological toxicity, reproductive toxicity, developmental toxicity, or immune system damage, among others [18].

CONCLUSION

For the environmental risk assessment of toxic organic chemicals, (Q)SARs play an important role in filling the data gap of environmental endpoints, decreasing experimental expense, reducing and replacing testing (especially animal testing), and assessing the uncertainty of experimental data. The analyses of results of this work have been shown that the cyclododec-2-en-1-yl ethers are persistent for some media (one exception is compound 1), bioaccumulative (without compound 3) and they are high toxic to fish. The high toxicity of the four ether compounds can be explained by their metabolic transformation (monooxygenase activation).

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