Environmental Research 154 (2017) 398–424

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

# Birds and flame retardants: A review of the toxic effects on birds of historical and novel flame retardants

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## ARTICLE INFO

*Keywords:*
Flame retardants
Bird
*In vivo*
*In vitro*
Adverse outcome pathway
Toxic effects

## ABSTRACT

Flame retardants (FRs) are a diverse group of chemicals, many of which persist in the environment and bioaccumulate in biota. Although some FRs have been withdrawn from manufacturing and commerce (e.g., legacy FRs), many continue to be detected in the environment; moreover, their replacements and/or other novel FRs are also detected in biota. Here, we review and summarize the literature on the toxic effects of various FRs on birds. Birds integrate chemical information (exposure, effects) across space and time, making them ideal sentinels of environmental contamination. Following an adverse outcome pathway (AOP) approach, we synthesized information on 8 of the most commonly reported endpoints in avian FR toxicity research: molecular measures, thyroid-related measures, steroids, retinol, brain anatomy, behaviour, growth and development, and reproduction. We then identified which of these endpoints appear more/most sensitive to FR exposure, as determined by the frequency of significant effects across avian studies. The avian thyroid system, largely characterized by inconsistent changes in circulating thyroid hormones that were the only measure in many such studies, appears to be moderately sensitive to FR exposure relative to the other endpoints; circulating thyroid hormones, after reproductive measures, being the most frequently examined endpoint. A more comprehensive examination with concurrent measurements of multiple thyroid endpoints (e.g., thyroid gland, deiodinase enzymes) is recommended for future studies to more fully understand potential avian thyroid toxicity of FRs. More research is required to determine the effects of various FRs on avian retinol concentrations, inconsistently sensitive across species, and to concurrently assess multiple steroid hormones. Behaviour related to courtship and reproduction was the most sensitive of all selected endpoints, with significant effects recorded in every study. Among domesticated species (Galliformes), raptors (Accipitriformes and Falconiformes), songbirds (Passeriformes), and other species of birds (e.g. gulls), raptors seem to be the most sensitive to FR exposure across these measurements. We recommend that future avian research connect biochemical disruptions and changes in the brain to ecologically relevant endpoints, such as behaviour and reproduction. Moreover, connecting *in vivo* endpoints with molecular endpoints for non-domesticated avian species is also highly important, and essential to linking FR exposure with reduced fitness and population-level effects.

## 1. Introduction

The current extent of chemical pollution has led some authors (e.g., Rockström et al., 2009) to conclude that the resulting damage to the environment is rapidly becoming irreversible. There are tens of thousands of human-made compounds in commerce and identifying those compounds that are most hazardous to the environment is critical. Some of the first chemical pollutants were organochlorine pesticides, such as the “Dirty Dozen”, and these were eventually regulated by the Stockholm Convention (http://chm.pops.int/). Flame retardants (FRs) are a diverse group of chemicals, many of which are added to plastics, textiles (e.g. furniture) and surface finishes (e.g. electronics), and used to inhibit or delay the spread of fire (Bergman et al., 2012; de Wit, 2002; van der Veen and de Boer, 2012). Moreover, additive FRs diffuse out of the polymers used in products and are released into the environment. Although FRs degrade during fire to release halogens, in turn quenching the fire, FRs are environmentally stable and hence persist. Due to the persistent nature of many FRs and their propensity to accumulate in biota, understanding the toxicity of flame retardants to wildlife is a critical

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http://dx.doi.org/10.1016/j.envres.2016.12.033
Received 11 August 2016; Received in revised form 17 November 2016; Accepted 20 December 2016

question in environmental research and policy.

There are several types of FRs: brominated FRs, chlorinated FRs, and organophosphate FRs or esters (OPEs). Some FRs are legacy FRs, whose production and use are regulated, banned or have been voluntarily withdrawn, but those compounds have been replaced with new compounds. Many of the legacy FRs contain bromines, which as halogens, share many toxic properties (Darnerud, 2003) with chlorinated compounds such as dichlorodiphenyltrichloroethane (DDT), polychlorinated biphenyl (PCB), and hexachlorobenzene (HCB), all chemicals listed under the “Dirty Dozen” (http://chm.pops.int/). In particular, polybrominated diphenyl ethers (PBDEs), especially the tetra- and octa-BDEs, increased exponentially in the environment prior to their phase-out in the mid-2000s (Elliott et al., 2005; Lindberg et al., 2004), and were eventually added to the Stockholm Convention (http://chm.pops.int/). PBDE levels have declined since many were phased out, but high levels of these bioaccumulative compounds still remain in top predators (Elliott et al., 2015; Fernie and Letcher, 2010; Guerra et al., 2011, 2012; Law et al., 2014). More recently, other FRs (e.g., hexabromocyclododecane (HBCD)) have been added to the Stockholm Convention, including the commercial mixture, deca-BDE, and short-chained chlorinated paraffins, that were listed in 2016 (http://chm.pops.int/).

As a result of the withdrawal of PBDEs from the market, alternative brominated FRs such as HBCD and non-brominated compounds such as OPEs were introduced and have increased in use. These alternative FRs have also been detected in increasing concentrations in the environment, with some observed at high concentrations in avian predators at high trophic positions in aquatic and terrestrial food webs (Chen et al., 2012a; Johansson et al., 2009; Lindberg et al., 2004). While some alternative FRs were subsequently assessed and regulated under the Stockholm Convention (e.g., HBCD, short-chained chlorinated paraffins), some remain in use, like a number of the OPEs. Even though several OPEs do not appear to bioaccumulate to the same degree as PBDEs, they were recently identified as priority chemicals for risk assessment by Environment and Climate Change Canada (formerly Environment Canada), in part because of their presence in biota (Greaves et al., 2014). Clearly, the toxicity of these novel compounds and other FRs is important to establish.

Birds are often used as sentinels for environmental contamination. Many of the trends in FR levels are derived from avian research and monitoring programs. Birds, especially those feeding at a high trophic position in the food chain, such as birds of prey, seabirds, and gulls, are particularly useful sentinels for monitoring flame retardants because 1) they can accumulate high levels of contaminants, 2) they integrate signals over large spatial and temporal scales, and 3) they often return to a central place (e.g., a nest site or breeding colony) where they may be accessed for sample collection and observed for some reproductive parameters. Because birds are often used in monitoring programs (Chen and Hale, 2010; Chen et al., 2012b), and have relatively high levels of pollutants making them particularly susceptible to potential effects of the chemicals, understanding of the toxicity of FRs and other chemicals in birds is strongly needed.

The FRs included in this review have been detected in the tissues of wild birds. Birds are used throughout the world for characterizing and monitoring FR levels (Abbasi et al., 2016; Chen et al., 2012a; Eens et al., 2013; Eulaers et al., 2014; Gómez-Ramírez et al., 2014;Jaspers et al. 2006). In a global review on PBDE contamination in birds, Chen and Hale (2010) reported that PBDE levels in terrestrial birds, in particular the chemical mixture deca-BDE which predominantly contains BDE-209, were highest in North America and China. In general, terrestrial birds had higher deca-BDE concentrations than aquatic birds (Chen and Hale, 2010), and the highest PBDE concentration reported in any wild bird was from a terrestrial apex predator, a Cooper's hawk (*Accipiter cooperii*) (Elliott et al., 2015). Both legacy and novel brominated FRs have also been reported in another terrestrial apex predator, the peregrine falcon (*Falco peregrinus*), in which the highest concentration of HBCD for any biota was reported in a peregrine egg (Guerra et al., 2012). Finally, novel OPEs have been detected in herring gull *(Larus argentatus)* eggs from the Great Lakes in North America (Chen et al., 2012a; Greaves and Letcher, 2014). In sum, the detection of a variety of FRs in multiple species of wild birds provides the ecological context for captive toxicity studies and the need for a review of the toxicity of FRs in birds.

Here we provide a critical review of the *in vitro* and *in vivo* toxic effects of flame retardants on birds reported to date (2016). Our goal is to use the Adverse Outcome Pathway (AOP) framework and apply it to avian toxicity research with flame retardants generally. The AOP is a tool that integrates knowledge relating to the links between a molecular initiating event, such as exposure to a chemical, and a chain of events at increasing levels of biological organization (Ankley et al., 2010). Specifically, we examine which endpoints showed consistent effects across chemicals and species in relation to the birds' exposure to flame retardants. We consider the most commonly reported endpoints, from molecular and hormone systems through behaviour to reproduction. Because of wide differences in methodologies, such as dosage levels and timing, we cannot use a strict meta-analysis. Rather, we use a weight of evidence approach where we calculate the proportion of studies reporting at least one significant effect for each endpoint.

## 2. Methods

### 2.1. Data search methods

We searched initially for the following keywords in Web of Science: ‘avian’ or ‘bird’ and ‘flame retardant’. This initial search allowed us to determine the most commonly reported endpoints. We then conducted subsequent searches with ‘avian’ or ‘bird’ and ‘flame retardant’ and each endpoint of interest. References from the publications collected from these searches were also collected until we were satisfied that all relevant references were included. In addition to experimental studies, we included field studies that examined correlations between tissue or plasma concentrations of flame retardants and endpoints of interest. Although we did not set a limitation to how far back we went in time, we only collected articles that were available electronically via the McGill University Web of Science portal. We included a total of 61 studies in our review.

### 2.2. Types of flame retardants

We included in our review, FRs that have been phased out but are still detected in the environment (e.g. PBDEs), FRs that are currently being phased out (HBCD), and FRs that are currently in use, such as 1,2-dibromo-4-(1,2-dibromoethyl)-cyclohexane (DBE-DBCH; formerly abbreviated as TBECH) and tetrabromobisphenol A (TBBPA). Although most of the studies in this review focused on brominated flame retardants (BFRs), some focused on OPEs such as tris (1,3-dichloro-2-propyl) phosphate (TDCIPP), tris(2-chloroisopropyl) phosphate (TCIPP), tris(2-butoxyethyl) phosphate (TBOEP), tris(2-chloroethyl) phosphate (TCEP), and tris(methylphenyl) phosphate (TMPP). Other FRs included in the review but to a lesser degree than those described above are: Dechlorane Plus (DP; also known as bis(hexachlorocyclopentadieno) cyclooctane), hexachlorocyclopentenyldibromocyclooctane (HCDBCO or DBHCTD), bis(2-ethlylhexyl)tetrabromophthalate (BEHTBP, now BEH-TEBP), 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE), decabromodiphenyl ethane (DBDPE), tetrabromobisphenol A bis(2,3-dibromopropyl ether) (TBBPA-BDBPE), tris(4-*tert*-butylphenyl) phosphate (TBPP), tris(2-ethylhexyl) phosphate (TEHP), tris(2-butoxyethyl) phosphate (TBEP), melamine (Mel), chlorendic acid (CA), bis(2-ethylhexyl) phosphate (HDEHP), vinyl bromide (VB), tricresyl phosphate (TCP), allyl 2,4,6-tribromophenyl ether (ATE), 2,2-bis(bromomethyl)-1,3-propanediol (BBMP), and tris(2,3-dibromopropyl) isocyanurate (TBC). In sum, we included in our review,