Toxic Equivalency Factors (TEFs) for Halogenated Aromatic Hydrocarbons in Wildlife

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Introduction

In recent years efforts have been made to formulate sets of toxic equivalency factors (TEFs) for the persistent and toxic group of environmental contaminants, the halogenated aromatic hydrocarbons (HAHs) [1-5]. The HAHs of major interest are certain polychlorinated dibenzo-*p*-dioxins (PCDDs), dibenzofurans (PCDFs) and biphenyls (PCBs), but also polychlorinated naphthalenes and brominated analogs of the above mentioned chemical groups. HAHs are present in the environment as complex mixtures of hundreds of identified and unidentified chemicals [6-8] whose relative concentrations differ across locations, among species and with time. The complex nature of the contamination in combination with great species differences in sensitivity to these compounds complicates the risk/hazard assessment of HAHs for wildlife. Therefore, a scientifically acceptable method to establish the hazard posed by these complex mixture as a whole is required to effectively perform hazard assessments under different environmental conditions. For this purpose, the toxic equivalency concept has been devised, including the consideration of species-specific TEFs.

The TEF concept

TEFs are used to calculate toxic equivalents (TEQs) for complex environmental mixtures of HAHs by multiplying the concentration of each HAH by its TEF, followed by summation of the products. To derive and apply TEFs appropriately, an understanding of the basic mechanism of action is essential. At the basis of the TEF concept lies the fact that several HAHs exert their toxicities via a common mechanism of action involving the initial binding of the compounds to a biological receptor (the Ah receptor) as a required first step [9-12]. The toxic potency of a given HAH is compared to that of tetrachlorodibenzo-*p*-dioxin (TCDD) and expressed as a ratio, the value of which is its TEF. Thus TEFs are indices of the rank-order of relative toxic potency of a given HAH and cannot be used to predict or describe absolute sensitivity of a given species to HAH exposure, without additional toxicological information.

Species-specific TEFs

TEFs are based on biological effects and, thus, dependent on numerous biological variables, such as species, strain, sex and age. Nevertheless, it appears that among the mammals studied so far, TEF values for specific HAHs are not dramatically different [5]. In fact, TEF values appear to fall within a range of about an order of magnitude. Considering the many other and often larger uncertainties when performing risk assessments, this is an acceptable range [13]. On the other hand, TEFs derived for fishes and birds appear to show somewhat greater differences when compared to mammals, but only for certain HAHs [14-18], indicating the need to formulate separate sets of TEFs for fish and birds.

TEFs in fish

Based on the ability of certain HAHs to induce the Ah receptor mediated induction of cytochrome P450 1A activity and gene expression, and early life stage mortality, it appears that several fish species are sensitive to TCDD-like compounds, with most studies performed in rainbow trout (*Oncorhynchus mykiss*) [16,19]. A major difference between fish and mammals is a lack of these responses in fish exposed to mono-*ortho*-PCBs [5]. As a result, TEFs for mono-*ortho*-PCBs in fish are considerably lower than those in mammals, which implies that the use of mammalian TEFs would overestimate the potential relative TCDD-like toxicity of complex mixtures to fish.

TEFs in birds

TEFs for HAHs have been derived in several avian species based on data from egg injection studies, studies with cultured avian hepatocytes and studies with cultured thymus cells. Various endpoints were taken into consideration, most notably embryo mortality and induction of cytochrome P450 1A. The bird species examined include the domestic chicken (*Gallus domesticus*), duck (*Anas plathyrynchos*), domestic goose, turkey (*Meleagris gallopavo*), pheasant (*Phasianus colchicus*), herring gull (*Larus argentatus*), common tern (*Sterna hirundo*), double-crested cormorant (*Phalacrocorax auritus*) and American kestrel (*Falco sparverius*) [14,20-22]. In general, TEFs for dioxins, furans and non *ortho*-PCBs based on EROD induction in birds are in the same range as those reported from mammalian systems. Exceptions are several PCDFs, such as 2378-TCDF [18,23], 23478-PCDF and 12378-PCDF [14], which appear to be more potent than TCDD in hepatocyte cultures from several species of birds. Birds, in contrast to fish, appear to show a more pronounced response to *mono-ortho* PCBs relative to TCDD. TEFs derived for PCB-105 and 118 in domestic chickens resemble those found in mammalian systems. However, based on CYP1A induction *in vitro*, certain wild avian species appear to be less responsive to mono-*ortho*-PCBs [14,21]. The domestic chicken, with its great sensitivity to TCDD-like compounds, appears to be an exception among avian species and may not be suitable as a general model for the derivation of TEFs for avian wildlife. When avian TEFs based on CYP1A1 induction are compared with those based on embryo mortality, the values correspond well. Thus, the relative potencies of these compounds as determined by CYP1A1 induction in cultured avian hepatocytes appear to be good predictors of their toxicity relative to TCDD in the developing avian embryo [21].

Use of TEFs in wildlife hazard assessment

TEFs have been applied successfully in a number of avian biomonitoring studies to associate exposure to TCDD-like HAHs with biological effects such as the induction of CYP1A, edema and adverse effects on growth and development [24-29]. The observed effects correlated better with TEQs than with any individual chemical, demonstrating the effectiveness of the TEF concept in these types of hazard assessments [30].

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