Phenolic Endocrine Disrupting Chemicals (Alkylphenols and Bisphenol A) in Asian Waters

Hideshige Takada, Miki Kanai and Yuki Hagino
Tokyo University of Agriculture and Technology, Japan

Phenolic endocrine disrupting chemicals (EDCs) are widely used in industrialized societies. Intensive surveys of the EDCs in industrialized countries during last several years demonstrated that phenolic EDCs are widely distributed in aquatic environments due to their widespread usage. However, very little information on the distribution and behavior of phenolic EDCs is available in South and South East Asia. Thus, we conducted monitoring of phenolic EDCs in the Asian waters. In the presentation, two aspects of the phenolic EDCs contamination in South East Asian waters will be introduced.

Phenolic EDCs in leachate from garbage dumping sites in South East Asia

Phenolic EDCs (NP, OP, BPA) were measured in leachates from 11 landfill sites in five Southeast Asia countries including Malaysia, Philippines, Thailand, Vietnam, and Cambodia. Extremely high concentrations of BPA ranging from 2.3 μg/L to 4300 μg/L were detected in the leachates. Combined with our measurement of natural estrogens (E1, E2, E3) in the leachates, estradiol-equivalent concentrations (EEQ) were calculated for all the target compounds and compared each other. In most leachates, contribution of BPA to total estrogenic activities was predominant over the other compounds including natural estrogens. Our monitoring demonstrated that leachates form garbage dumping sites could be major contributors of EDCs to aquatic environments in South East Asia. More extensive monitoring focusing on the dumping sites and surrounding environments are urgently necessary as well as installing sustainable leachate treatment systems to the dumping sites.

Accumulation of phenolic EDCs in mussels

Using mussels and seawater collected from Tokyo Bay, bioconcentration factors (BCFs) was determined for the phenolic EDCs. In mussel samples, NP was most abundant with the concentration range from 47 to 1347 ng/g-dry tissue. NP concentrations were several times higher than PCBs. OP and BPA concentrations were one to two orders of magnitude lower than NP. Based on the EDC concentrations in the seawater and the mussel tissue, BCFs were calculated. Lipid-base BCF of NP, OP, and BPA was ~10³, ~10², and ~10⁰ respectively. These values were similar to octanol-water partition coefficients (Kow) for individual compounds, indicating that the EDCs are bioconcentrated through their partitioning between the biological lipid and the surrounding water.

Green mussel samples collected from India, Indonesia, Malaysia, Singapore, Thailand, Vietnam, Cambodia, and the Philippines were analyzed for the phenolic EDCs. At several locations in S&SE Asia, elevated concentrations of EDCs were observed. The high NP concentrations up to 600 ng/g-dry tissue found in Malaysia, Singapore, the Philippines, and Indonesia were comparable to those in Tokyo Bay. BPA concentrations found in one location in India exceeded the highest concentration in Tokyo Bay. No elevated EDCs concentrations were observed in Vietnam and Cambodia, probably due to the lower levels of industrialization in those countries.
Human and Wildlife Exposures to Persistent Brominated Flame Retardants

Åake Bergman
Stockholm University, Sweden

Brominated flame retardants (BFRs) have become increasingly important in the technosphere during the last two decades. Still the BFRs are only making up less than twenty per cent of all flame retardants being used. The production volumes are still high, exceeding 200,000 tons annually on a global scale. Among approximately twenty BFRs in production three basic structures form the basis for the major BFRs. The far most used BFR is tetrabromobisphenol A (TBBPA) and its three neutral derivatives, diallyl, dibromopropyl and diglycidyl ether, respectively. The second most used BFR is DecaBDE, almost entirely consisting of perbromodiphenyl ether (BDE-209), and third hexabromododecane (HBCDD). Other BFRs of interest are the OctaBDE and PentaBDE, both consisting of PBDE mixtures with different content of bromine. The use of these two PBDE products has been regulated within EU during 2004. Still all PBDEs are present in a huge number of commercial products that are slowly moving towards their end of life. The BFRs are distributed to the environment and humans are exposed to BFRs both directly via inhalation at home and at work and indirectly via their food. The major BFRs present in wildlife, domestic animals and in humans are PBDEs including all PBDEs up to the decaBDE and HBCDD, while TBBPA is less abundant in humans and in wildlife.

The human exposure to PBDEs, as measured in blood serum or plasma, and in milk, is different in different parts of the world. Humans living in Japan and Europe have in general low concentrations unless the persons are subjected to occupational exposures. The general populations have in general below 10 ppb lipid base concentrations while the situation is much different in North America with a large number of subjects with levels above 100 ppb, even up above 1000 ppb has been reported. The PBDEs have been found to increase in mothers’ milk from different countries. Recently there are strong indications of a trend shift in the PBDE pattern showing a hexaBDE, BDE-153, to be the major PBDE congener in humans, instead of BDE-47 - a tetrabrominated diphenyl ether. DecaBDE is bioavailable and the Swedish concentrations are nowadays similar to BDE-47. BDE-209 is indicated to degrade to lower brominated congeners in humans and it has a half-life of approximately 14 days in man. BDE-209 has become more commonly reported in mammals, fish and birds as more laboratories have started to look for it. Since present in fish, chicken and dairy products BDE-209 is also ingested by humans via the food. Human levels of BDE-209 above 100 ppb has been reported both for occupationally and randomly exposed humans. Increasing time trends have been shown for HBCDD in guillemot eggs from the Baltic Sea. No temporal trends are reported for HBCDD in humans even though reported in people from Sweden, The Netherlands and Mexico. Several of the BFRs have been associated with endocrine related effects.
PCB Metabolites in Humans with Focus on OH-PCBs and MeSO$_2$-PCBs

Åake Bergman
Stockholm University, Sweden

Shortly after PCBs first were identified as ubiquitous environmental contaminants they were also found to undergo metabolism and forming hydroxylated PCBs, more correctly referred to as polychlorobiphenylols (OH-PCBs). However, these metabolites were initially regarded as excretion products and consequently of less importance. It was not until the 1980s’ when OH-PCBs were found to be retained in the body they become more interesting. OH-PCBs are excreted and may be present in the intraluminal uterine fluid but most important is their retention in the blood. OH-PCBs are retained in fish, bird, and mammalian blood at high concentrations. Hitherto approximately fifty OH-PCBs have been identified in human blood with some five congeners being the most prevalent metabolites in the blood. These are 4-OH-CB107, 3-OH-CB138, 4-OH-CB146, 3-OH-CB153 and 4-OH-CB187, metabolites that are present in concentrations of up to hundreds of ppb, e.g. the last congener is present at median levels of 100-150 ng/g l.w. in human serum from subjects sampled in Slovakia and in the Faroe Islands. Individual OH-PCB concentrations in humans and in wildlife are often higher than the concentrations of individual PCB congeners, of course excluding the most prevalent PCB congeners. 4-OH-CB107 and 4-OH-CB187 have blood half-lives in rats of 4 and 15 days, respectively, that indicate that we can expect the latter to have between 2 and 3 months in humans. These two OH-PCBs have been more thoroughly investigated in relation to its endocrine related effects and found to influence the thyroid hormone homeostasis and oestrous cyclicity.

PCBs do undergo Cytochrome P450 mediated oxidations leading to the formation of reactive arene oxide intermediates. These arene oxides may be rather stable as in the case of 2,2',5,5'-tetraCB 3,4-oxide while much more reactive in others. The arene oxides of PCBs may react with biomacromolecules or undergo further oxidations to quinones, metabolites that similarly to the arene oxides are very electrophilic species. The arene oxides are precursors of PCB dihydrodiols, OH-PCBs, formed with or without a 1,2-shift, and PCB methyl sulfones (MeSO$_2$-PCBs) after reaction with glutathione, mercapturic acid pathway transformation, C-S-lyase cleavage of the sulphur-cysteine carbon bond, methylation and oxidation.

MeSO$_2$-PCBs are formed from the most reactive PCBs, compounds with at least one meta-para-position free for oxidation. Hence the metabolites have a higher persistency than the maternal PCB compound. Still, both wildlife and human concentrations of MeSO$_2$-PCBs are lower than for the most abundant OH-PCBs. MeSO$_2$-PCBs are present at low ppb or less on a lipid weight basis in humans even when exposed to PCBs. This makes the occurrence of these metabolites in humans of less importance than the OH-PCB metabolites. Still, it is interesting to note that several MeSO$_2$-PCBs are optically active with a total dominance of one atropisomer over the other, as observed in e.g. grey seals. The PCB methyl sulfones have some very different enzyme induction properties; they accumulate specifically in human and wildlife lungs and in particular in the liver.
Rating Risks of Chemical Exposures: Dose and Time

Robert I. Krieger
University of California, Riverside, USA

Responses to chemical exposures will fundamentally be determined by dose and time. Environmental pesticide exposures are of low magnitude relative to harmful levels and of short duration, even in the workplace.

Risk characterization is the latest means used in product development and regulation to evaluate and to regulate chemical technologies including pesticides. The strategy includes risk assessment, risk management, and risk communication—some persons consider these processes “Risk Assessment.” The process including determination of how much and frequency of exposure formalizes safety evaluations of food residues that have occurred for over 100 years in the United States, applicator and mixer/loader exposures of the past 50 years, harvester field reentry (now “entry”) during the past 30 years, and general environmental residues since the general availability of gas liquid chromatography and other advanced analytical techniques and publication of Silent Spring. Still more and more concern continues to be made of lower and lower amounts as analytical chemistry continues to contribute record of “findings” of trace analytes from diverse media—information that sometimes exercises a strong role in defining the hazardousness of many aspects of modern life, particularly public policy making.

The effectiveness of management strategies concerning reduction of current pesticide exposures and risks contrasts sharply with a listing of previously acceptable chemical exposures. General education initiatives at all levels concerning the chemical nature of the environment and the fate of chemicals in exposed persons will be required to improve risk communication. Consumers, workers, and the environment will remain the focus of Risk Assessment and default assumptions will be replaced by more defensible measures of exposure and effect. A major strength of the risk assessment process is establishment of common denominators for weighing the relationship between harmful and benign chemical exposures related to use of chemical technologies.
Multi-Component Mixtures of Endocrine Active Chemicals - Experimental Requirements and Recent Test Results

Andreas Kortenkamp
University of London, UK

Although the necessity of evaluating multi-component mixtures of endocrine disrupting chemicals is widely acknowledged, the prospect of approaching this topic experimentally is often dismissed because it is deemed as "too complicated". However, the last few years have seen considerable progress in this field, and this talk will give an overview of recent test results from our laboratory.

We have recorded concentration-response relationships for endocrine active chemicals in in vitro assays including the yeast estrogen screen (YES) and the E-Screen assay. This information was used to make predictions of the effects of multi-component mixtures composed of more than 10 components, assuming additive combination effects. It was found that the experimentally observed responses were in good agreement with the model predictions. This suggests that a large number of estrogenic chemicals are able to act together in an additive fashion.

Taken together, our test results show that estrogenic chemicals produce combination effects even when they are present at concentrations that will not yield measurable responses upon individual administration. Furthermore, sufficiently large numbers of xenoestrogens are able to modulate the effects of steroidal estrogens. This challenges the widely held view that endogenous steroidal estrogens are too potent for xenoestrogens to elicit noticeable responses, and therefore are of negligible concern.