

Xenoestrogens and Our Chemical Environment:  
From Baby Bottles to Thermal Paper  
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Xenoestrogens are defined as chemicals occurring in the environment mimicking the effects of bodily produced estrogens. These can be synthetically produced steroid estrogens like those found in birth control, or industrial chemicals such as bisphenol A (BPA) which is used in plastic production.<sup>1</sup> Estrogens are active at very small concentrations in blood; on the order of ng/L quantities.<sup>2</sup> Xenoestrogens when paired with high persistence, even though not immediately toxic, pose threat to wildlife in the form of infertility, and developmental problems. It is also hypothesized that fetal exposure to estrogenic agents may lead to impaired development of both male and female human reproductive systems.<sup>3</sup> To use an analogy, the oral contraceptive pill is made of progesterone and estrogen and consumed by women, yet it still prevents pregnancy. When high enough concentrations of xenoestrogens are in groundwater, a similar effect of decreased fertility is observed for male and female aquatic life in general.

Xenoestrogens fall under a large class of compounds known as endocrine disruptors. These compounds are of particular importance when the endocrine, reproductive and immune systems are being developed in mammals and aquatic life.<sup>4</sup> This is most important for the fetal stage in humans and for infants. Endocrine disruptors can be persistent and bioaccumulate.<sup>5</sup> This is even more cause for concern for breast feeding mothers because of the lipophilicity of xenoestrogens and high fat content of breast milk. However, even formula-fed infants are in some cases found to have higher concentrations of BPA than adults.<sup>6</sup> This suggests the routes of exposure are not limited to the oral consumption of bioaccumulated xenoestrogens. The bottom line is that the effects of xenoestrogens have less to do with the estrogenicity of the compounds, and more to do

with their endocrine disrupting effects. Agonism of the E2 receptor is not the only effect of xenoestrogens. Some also serve as antagonists as well, limiting the effect of endogenous estrogens.

Endocrine disruptors are typically neither mutagens or acute toxicants at ambient concentrations. This is unfortunate as regulatory agencies in America assess risk mainly by carcinogenicity, acute toxicity, and immediate mutagenicity.<sup>5</sup> This leads people to believe that endocrine disruptors do not cause harm to wildlife or humans. Human infertility can first be assessed in early adulthood so any effective study on the effects of xenoestrogens on human reproductive system must begin in the embryo stage and take over a decade.

Xenoestrogens originate from a variety of sources including pesticides, cosmetics, incinerators, hormone therapy and the combined oral contraceptive pill. Notably, all of these products end up in the water. Pesticides run off when it rains, cosmetics get washed down the drain, we excrete consumed estrogen in our urine, and incinerators produce the particulate matter that rain is formed from.<sup>5</sup> The pesticide dichlorodiphenyltrichloroethane (DDT) has only been banned due to its harm to the American bald eagle rather than its xenoestrogenic effects.<sup>7</sup> In general, pesticides are not risk assessed by endocrine disruption, meaning all banned pesticides, herbicides, etc. that happen to be xenoestrogens were banned for some other reason. This is problematic as it gives the false perception that these compounds are bad only because they are carcinogens or because of acute toxicity.

Little research has been done into what effects different xenoestrogens have with each other. Only small-scale pairings have been tested and have shown no anti-synergetic effects, meaning the effects are likely cumulative. One study of the effects of two mycoestrogens were found to be synergetic in human cells showing that combination effects must be considered when assessing the risk of different prominent xenoestrogens in the environment.<sup>8</sup>

BPA has been a controversial chemical since the late 2000s due to our production volume and suspected toxicity of the substance. Little was known about the long-term exposure to the substance at the time. 10 million tons of BPA are expected to be produced worldwide in 2022.<sup>9</sup> The average daily BPA intake is 46.8ng/kg-day for Americans age 6 and up in 2003 and 200-500ng/kg-day in 2009. However, hormones are active at microgram per liter concentrations in the blood. For example, the average estradiol concentration in men is 10-40ng/L. Infants were the largest consumers of BPA by body weight per capita in 2009.<sup>6</sup> Since the developmental stages are the most sensitive time for endocrine disruptors, BPA has since been banned in baby bottles in the EU and Canada due to health risks. BPA-free plastic has become increasingly common in food containers. However, humans can still be exposed through drinking water, inhalation, and through skin contact of things like thermal paper receipts and cosmetics.

Methods to detect estrogens in the environment have only recently been invented due to the low concentrations at which they exist. In the late 90s, a solid phase extraction method to detect estrogen in the groundwater was published.<sup>10</sup> Our research involves perfecting a method of HPLC-MS for detection of different sulfated estrogens specifically in cow waste. Estrogens in their sulfated form persist much longer in the environment than in their unconjugated form due to the polarity of the sulfate group. This means they effectively have a stronger effect on wildlife since sulfatase *in vivo* converts sulfated estrogens into their active forms.<sup>11</sup> In consolidated animal feeding operations (CAFOs), concentrations of estrogens in runoff are expected to be much higher than ambient concentrations posing threat to wildlife downstream.

One study in Beijing tested the wastewater from a pharmacy factory mostly producing contraceptives and found 1.0ng/L effluent and 85ng/L influent concentration of estradiol (E2). This was using an LC-MS-MS method to simultaneously detect concentrations of four different

estrogen compounds. Based on similar studies from sewage treatment plants in Italy, Brazil, Japan and the Netherlands, influent concentrations of E2 were similar: between 12-94ng/L across all studies.<sup>4</sup>

## References

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