Phthalates as Endocrine Disrupters

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ABSTRACT

Recent studies on the effects of phthalates in the endocrine system have led to conflicting results. We hypothesize that phthalates are disrupt the function of the endocrine system. Phthalates are a family of man-made compounds used as an inexpensive way to increase the pliability of plastics during the manufacturing process of plastics. Phthalates readily partition into the environment. Thus, people are constantly exposed to these synthetic materials. Our literature-based research is based on research previously done on the effects of phthalates on the endocrine system, growth, and development. Phthalates are believed to cause an early onset puberty, which suggests that they interact with the endocrine system.

BACKGROUND

Phthalates (Figure 1) are man-made chemicals that are commonly used in a variety of industries. They are generally consumed by the plastics industry to enhance the flexibility and durability of the polymeric materials. However, phthalates are also found in household products such as modeling clays, paint, and cosmetics. Due to their lipophillic nature, phthalates may contaminate food products such as meat, butter, and milk because they are stored in plastic containers.

Phthalates are noncovalently bonded to the plastics with which they are mixed with. This weak chemical bond facilitates the release of phthalates into their surrounding medium. As phthalates break down, commonly due to an increase in heat, the release of phthalates increase.

Due to their chemical nature, these harsh compounds pose health risks to the public, especially as endocrine disrupters in pre-adolescents.

Recent studies suggest that phthalates may be endocrine disruptors. Endocrine disruptors are chemicals that interfere with production, release, transport, metabolism, binding, action, or elimination of natural hormones responsible for homeostasis and essential for normal growth and development. One type of endocrine disruptor is the man-made estrogen-mimicking chemicals, the so-called xenoestrogens (Figure 2). Phthalates fall into the xenoestrogens classification scheme, but their specific function as weakly estrogenic compounds remains controversial.

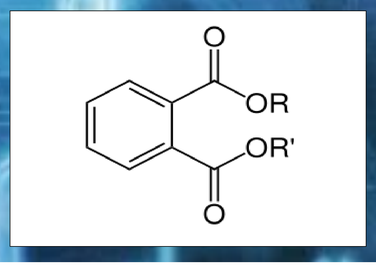

Figure 1: General Phthalate Structure (source: [1])

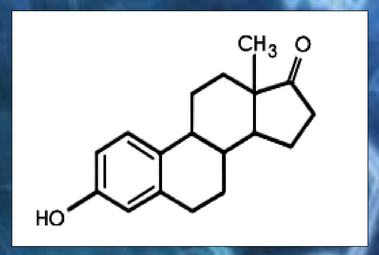

Figure 2: Estrogen

ESTROGENIC ACTIVITY *IN VITRO*

In one study [2, 3], thirty-five phthalates esters with variable structure and behavior were analyzed *in vitro* using a recombinant yeast screen to determine their estrogenic activity. The human estrogen receptor gene was ligated into the main yeast genome. This gene can be expressed upon the binding of estrogen, or in this case, a weakly estrogenic phthalate compound, which then controls the molar concentration expression of the reporter gene Lac-Z. This expression of the Lac-Z gene ultimately produces Ethanol galactosidase, an enzyme, which is secreted into the surrounding medium. Upon secretion into the DTDP medium, a color change from yellow to red can be observed. This red color can be measured in terms of absorbance (See Figure 3).

Some phthalates generated a dose-dependent increase in galactosidase production in the yeast screen, indicating weak estrogenic activity. Figure 3 shows other environmental estrogens that were used as to relate the importance of the estrogenic activity of the phthalates. The estrogenic activity in the yeast screen of phthalate esters at concentrations ranging from 10^{-3} to $5x10^{-7}$ M, compared to 17α-estradiol. The phthalates with the greatest absorbance were BBP, DBP, and DIBP. All of the phthalates that showed activity were weak estrogens. The most potent, BBP, was approximately 1 million-fold less potent than estradiol (Table 1), making it less potent than other environmental estrogens such as bisphenol A.

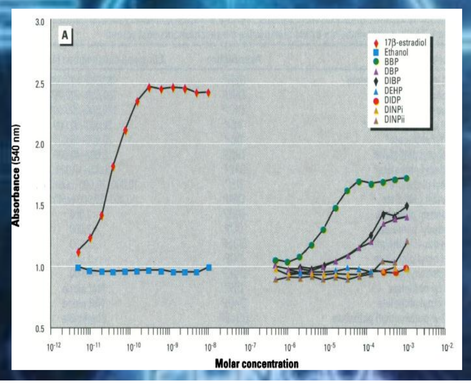

Figure 3: Estrogenic Activity of Several Phthalates (source: [2])

Chemical	Structure	Approximate potency[a,b]	Maximum response (%)[b]
17β-Estradiol		1	100
Diethyl phthalate		0.0000005	30
Dibutyl phthalate		0.0000001	35
Diisobutyl phthalate		0.0000001	30
Butyl cyclohexyl phthalate		–	20
Butyl benzyl phthalate		0.000001	50
Diphenyl phthalate		–	10
Isohexylbenzyl phthalate		–	20
Diisononyl phthalate		–	15
Ditridecyl phthalate		0.0000001	95

Table 1: Phthalates Showing Activity in the Yeast Assay (source: [2])

ESTROGENIC ACTIVITY *IN VIVO*

In a separate study with laboratory animals [4], it has been shown that certain phthalate plasticizers have a carcinogenic effect. Studies on male lab rats showed a decreased level of testosterone, which leads to a decreased sperm count, infertility, undescended testes, malformation of the penis, and other reproductive deformities.

In Puerto Rico, girls as young as six to twenty-four years old experience premature breast development [5]. The girls were tested for phthalates in their blood, and the results displayed that phthalates were indeed present. Because Puerto Rico is an island with a tropical climate, phthalates are easily leaked into the food supply. It has to import its food, and since the weather is warm, the stability of plastics decrease, which results in a higher rate of phthalates leaching into the food supply.

PHTHALATES AND THE BLOOD SUPPLY

Since phthalates are easily miscible in organic solvents such as plasma and saliva, they are easily ingested or absorbed, especially during medical procedures where utensils made with plastics are employed. Studies have shown that red blood cells survive better in blood bags made with PVC compared to glass containers [6]. Within twenty-four hours, the plastic bags contaminated the blood with 2.5 milligrams of DEHP per liter of blood. DEHP is thought to be potentially harmful, but studies have shown that the chemical is beneficial to the production of cholesterol and phospholipids during storage. DEHP has been shown to reduce the death of red blood cells.

CONCLUSION

Our literature research, supports the hypothesis that phthalates interact with the endocrine system. Phthalates are weak estrogenic chemicals that may play a smaller role as endocrine disrupters. Research shows that phthalates cause developmental problems in males and cause early development of the breasts in females. Although phthalates are generally thought of as hazardous to human health, phthalates also have benefits such as improving the shelf life of blood.

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