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Characterization of estrogenic and androgenic activity of phthalates by the XenoScreen YES/YAS *in vitro* assay

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Highlights

- An assessment of endocrine potential of phthalates by an *in vitro* yeast test
- Phthalates exhibit strong anti-estrogenic and anti-androgenic activity
- *In vitro* testing is an important element of tiered toxicological studies
- Further investigations of phthalates' metabolites and mixtures endocrine potential are needed

Abstract: The presented study investigates and compares the estrogenic and androgenic activities of commonly used diesters of phthalic acid (phthalates) using the XenoScreen YES/YAS assay. Phthalates are commonly used plasticizers in polymers dedicated for i.e. food and drug containers. Since phthalates are not chemically bonded to the polymer, they can leach or migrate from the polymer. Therefore, phthalates are identified as contaminants in a variety of consumer products. Investigation of estrogenic and androgenic activities of phthalates (DEP, DBP, BBP, DEHP and DINP) showed no significant effect of tested substances either on hER α or hAR receptors. Phthalates exhibited strong anti-estrogenic (IC₅₀ for BBP = 8.66 μ M, IC₅₀ for DEHP = 3.61 μ M and IC₅₀ for DINP = 0.065 μ M) and anti-androgenic (IC₅₀ for BBP = 5.30 μ M, IC₅₀ for DEHP = 2.87 μ M and IC₅₀ for DINP = 0.068 μ M) activities.

Key words: endocrine disrupting chemicals, phthalates, yeast test, androgenic potential, estrogenic potential

1. Introduction

According to the World Health Organization (WHO) endocrine disrupting chemicals (EDCs) are exogenous substances or mixtures that cause changes in the functioning of the endocrine system, thus, possibly, causing adverse health effects in exposed organism, its progeny, or (sub) populations (*WHO | State of the science of endocrine disrupting chemicals - 2012, 2016*). Endocrine disruption is a set of different possible mechanisms that can lead to disruptions in a normal functioning of the endocrine system. The basis of hormonal disorders can be both interference in the processes of binding hormone receptors or interference with the production, transport or metabolism of endogenous hormones (Bergman et al., 2012; Diamanti-Kandarakis et al., 2009; Kortenkamp et al., 2012). Some EDCs are hormone receptor agonists, meaning that they bind to hormone receptors and activate gene transcription (Baker, 2001; Dietrich et al., 2013; EFSA, 2010; Soto et al., 2006). Such substances will mimic the properties of endogenous hormones. However, their action does not necessarily lead to the same molecular events or biological outcomes, as endogenous hormones do (European Food Safety Authority, 2013). EDCs can also act as antagonists of the hormone-receptor, blocking hormone receptors, thus blocking gene transcription.

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