



The environmental contaminants, tributyltin and bisphenol S, alone or in combination, harm the hypothalamus-pituitary-gonadal axis and uterus

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ABSTRACT

Endocrine disrupting-chemicals (EDCs) are chemical compounds found in the environment that can have adverse impacts on human health. Among these agents are tributyltin (TBT) and bisphenol S (BPS). TBT is used in anti-fouling paints, and its indiscriminate use has health repercussions. BPS is found in plastic products and marketed as a safe alternative to bisphenol A (BPA). Little is known about the effects resulting from interactions between different EDCs on the organisms. The aim of this study was to analyze changes induced by exposure to these compounds in hypothalamic-pituitary-gonadal (HPG) axis and uterus. We divided four groups: Control, TBT 100 ng kg⁻¹.day⁻¹, BPS 50 µg kg⁻¹.day⁻¹, and the group simultaneously exposed to TBT and BPS. Rats were gavaged for 15 days and euthanized in the estrus phase. All EDCs groups showed uterus with cellular hyperplasia, glandular degeneration, increased epithelial thickness, and vacuolization. In the ovaries, there was an increase in atretic follicles in all EDCs groups. In the hypothalamus, the group exposed to the mixture showed an increase in the *GnRH* gene. In the blood, all EDCs groups had reduced levels of FSH and LH. Additionally, the BPS and mixture groups exhibited reduced levels of prolactin. Therefore, we suggest that exposure to these agents may contribute to damage to the female reproductive system, and that doses considered safe by regulatory agencies need to be reassessed.

1. Introduction

Endocrine disrupting-chemicals (EDCs) are xenobiotic substances (or mixtures of substances) that interfere with any aspect of hormonal action and disrupt the homeostasis of the endocrine system of an intact organism, its progeny or a (sub)population (Zoeller et al., 2012; Demeneix et al., 2020). Like other environmental pollutants, these

substances can be found in water, food, soil, household objects, medical materials, cosmetics, among others. With the increase in the production of these chemicals and also chronic diseases, several authors describe that the effects of exposure on human and environmental health can be vast (Heindel et al., 2015). Still, due to the wide structural and chemical differences between these agents, it is difficult to describe the mechanism of action of each of them, which in turn makes it difficult to

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