

The comparison of the influence of bisphenol A (BPA) and bisphenol S (BPS) on the enteric nervous system with particular emphasis of the cholinergic neurotransmission within the colonic myenteric plexus

Bisphenols are one of the most widespread toxic substances in the human environment. They are commonly used in the production of plastics, so, they are present in various everyday objects like bottles, thermal paper and food can linings. Until recently, the main bisphenol used in plastic production was bisphenol A (BPA). However, numerous scientific studies have shown that BPA is harmful for a living organism, mostly affecting the digestive tract, central nervous system, reproductive organs, immunological system and hormonal balance. For that reason many countries introduced restrictions to the application of BPA in some products, especially in goods intended for children. Therefore, BPA is being replaced by other substances, which are considered as safe for humans and animals. The most widely used substitute for BPA is bisphenol S (BPS). However recently, it has been reported that BPS can also have a negative impact on endocrine, gastrointestinal (GI) and reproductive systems. It should be emphasized that the exact mechanisms connected with influence of BPS on living organisms have not been fully elucidated, and the impact of this substance on the peripheral nervous system has not been studied at all.

Due to the fact that bisphenols mostly get into the organism through the digestive tract, first of all they have to break the intestinal barrier, wherein the important component is the enteric nervous system (ENS). It is relatively well known that ENS may undergo structural, functional or chemical changes in response to various physiological and pathological agents which mostly manifest as fluctuations in the expression of neuronal active substances.

Previous studies and preliminary investigations (conducted at Laboratory of Pharmacology and Neurobiology / Center for Drug Discovery and Innovative Medicines (MedInUP), ICBAS - University of Porto (Portugal) by the project coordinator Krystyna Makowska) have shown that BPA and BPS intoxications change intestinal motility and acetylcholine release, but the mechanisms underlying this effect remain elusive. It should be pointed out, that acetylcholine (ACh) is the most important excitatory neurotransmitter in the ENS. The aim of the planned studies will be the comparison of the influence of BPA and BPS on neurochemical characterization of the neurons and glial cells within enteric nervous system as well as Cajal cells in the selected parts of the GI tract.

Moreover, functional isolation of the different components of the tripartite myenteric synapse, comprising the nerve terminal, the glial cell and the interstitial cell of Cajal (ICC), which might be affected by both BPA and BPS, will be done in atropine plus nifedipine paralyzed preparations using specific cell activity inhibitors, such as tetrodotoxin, fluoroacetate and mibefradil, respectively.

It should be pointed out that during the planned studies low doses of BPA and BPS will be used. The use of this strategy may be favorable because, contrary to the reported actions of high concentrations of bisphenols, knowledge concerning the harmful effects of low doses of these substances on the living organism is very scanty and fragmentary. Moreover, because BPS passes to water and food to a lesser extent than BPA, humans and animals are more often vulnerable to relatively low doses of this substance. Emulating exposure to low doses of BPS, results will determine whether it is safe or neutral for the GI tract. The purpose of the project is to contribute to establish a safe daily dose of BPS in the mouse, which can later on be extrapolated to humans in order to establish limitations to human food and water contamination by BPS (at present such regulations do not exist). Knowledge concerning the negative impact of BPS on living organisms will certainly ameliorate human public health.

To sum up, the aim of planned investigations will be the comparison of the potency of BPA and BPS on the morphology and functions of the ENS in different regions of the GI tract. The planned studies will allow to increase awareness of mechanisms connected with impact of BPA and BPS on the living organism, what (due to a broad dissemination of bisphenols in the environment) is important for public health and prevention of diseases connected with the excessive exposure to these substances.