

BISPHENOL S ON PROLIFERATION AND MIGRATION OF REPRODUCTIVE CELLS

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ABSTRACT

In response to the growing concern about the negative impacts of Bisphenol A (BPA) on human health, BPA-free products made with substitute chemicals were manufactured. Bisphenol S (BPS) is one of the most widely used replacements for BPA. However, BPS may not be safer than BPA. Studies now show that BPS also exhibits endocrine-disrupting activities similar to BPA. BPS is obesogenic, cardiotoxic, neurotoxic, and immunotoxic. Nonetheless, there is very little understanding if this chemical is reprotoxic or can promote protumorigenic effects. This study addressed these concerns. It aims to determine whether BPS induces proliferation and migration of the human endometrial adenocarcinoma (Ishikawa) cell line and mouse reproductive tissues. Unregulated proliferation and migration are hallmarks of disease development and progression, especially in reproductive tissues. Further, cetaceans, known as sentinel species of the marine environment, were also utilized to explore reproductive diseases associated with endocrine-disrupting chemicals such as BPA and BPS. Results of this study showed that BPS could increase cell proliferation and stimulate migration in Ishikawa cells in association with the upregulation of estrogen receptor beta (ESR2) and vimentin (VIM). In addition, mice exposed to BPS enhanced the proliferation of ovarian surface epithelium and showed a significantly higher mean number of endometrial glands within the endometrium. Further, instances of adenomyosis or migration of the endometrial glands to the myometrium of mice were also observed. The collected reproductive tissues of cetacean species also showed phenotypes that can be associated with the effects of BPS as observed in the laboratory setting using a mouse model. Overall, *in vitro* and *in vivo* results obtained in this study showed that BPS could significantly promote endometrial epithelial cell proliferation and migration, a phenotype also observed with BPA exposure. Hence, the use of BPS in BPA-free products must be reassessed, as it may pose adverse reproductive health effects to humans and the environment.