## **Abstract**

Bisphenols are widely utilised in the production of polycarbonate plastics and epoxy resins. Many recent studies indicate that bisphenols can cause adverse side effects in humans, including reproductive disorders such as difficulty conceiving, polycystic ovary syndrome, precocious puberty, and reduced semen quality. They may increase the risk of breast and ovarian cancer and endometriosis. However, not all of these disorders have yet been confirmed in animals, including pigs. Therefore, the primary objective of the study was to expand knowledge on the effect of bisphenol A (BPA) and its analogues (BPAF, BPF, and BPS) on uterine contractility in pigs with different hormonal statuses (sexually immature gilts, cyclic gilts, and gilts in early pregnancy). Furthermore, since the mechanism of action of bisphenol A in the uterine muscle is not fully understood, an attempt was made to determine the contribution of key mechanisms (cholinergic, adrenergic, and noncholinergic/nonadrenergic) that regulate uterine contractility to the relaxant effect of BPA in gilts.

BPA caused a significant decrease in contraction amplitude, frequency, and tension in all study groups. BPF caused a decrease in the amplitude and frequency of contractions in all groups, as well as a decrease in tension in the early pregnancy group. BPAF also caused a significant decrease in all studied parameters in all animal groups, but the greatest changes were observed in the uterine muscle of immature pigs. BPS caused the greatest decrease in tension and amplitude of contractions in the uterine muscle of early pregnancy animals and the frequency of contractions in the uterine muscle of immature animals.

BPA administered after incubation with Krebs-Ringer solution (K-Rs), sodium nitroprusside (SNP), acetylcholine (ACh), and N-ω-nitro L-arginine methyl ester hydrochloride (L-NAME) significantly reduced uterine tension compared to the period before administration of the test substances. Contraction amplitude was significantly reduced in uterine muscle pretreated with SNP, K-Rs, ACh, epinephrine, phentolamine, L-NAME, and methylene blue (MB), and then stimulated with BPA. BPA administered after incubation with ACh, atropine, SNP, epinephrine, bupranolol, MB, phentolamine, and L-NAME significantly reduced the frequency of uterine contractions. BPA also significantly reduced the AUC following pretreatment with atropine, SNP, and L-NAME, as well as K-Rs, ACh, epinephrine, phentolamine, bupranolol, and MB.

The results indicate that BPA, BPF, BPAF, and BPS all exert a relaxing effect on the porcine uterine muscle, but these changes depend on the physiological state of the animals.

Furthermore, the mechanism of action of BPA in the porcine uterine muscle is complex, and the ultimate response to BPA results from multiple overlapping mechanisms of action.