Effects of DEHP on Progesterone Synthesis in FSH-stimulated Human Granulosa Cells

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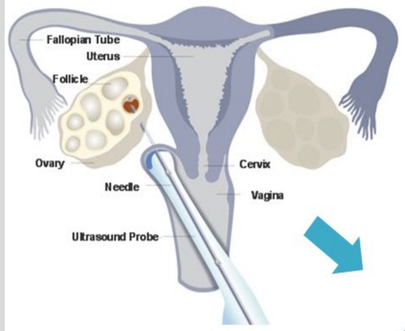
INTRODUCTION & OBJECTIVES

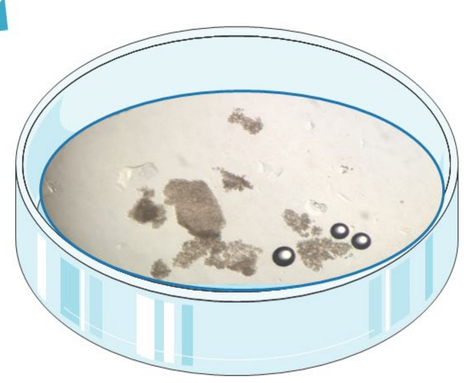
Infertility is a major reproductive health problem today that negatively affects many couples worldwide. Based on the predictive model of the world population, it is estimated that 72.4 million women are currently infertile. Given the short time frame, genetic changes cannot explain infertility. Endocrine disrupting chemical (EDs), beside smoking and age, may be one of the most important risk factors.

Di-(2-ethylhexyl) phthalate (DEHP) is categorized as an endocrine disruptor and classified as a chemical of high concern. It has been shown that DEHP can have adverse effect on the function of the female reproductive system. DEHP alters human ovarian function by disrupting the follicle stimulating hormone (FSH)-stimulated estradiol production in granulosa cells. However, it remains unknown whether DEHP can affect the progesterone production in human granulosa cells. The aim of this study was to investigate the effects and the potential mechanism of DEHP action on the basal and the FSH-stimulated progesterone production in human granulosa cells.

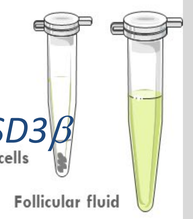
MATERIAL & METHODS



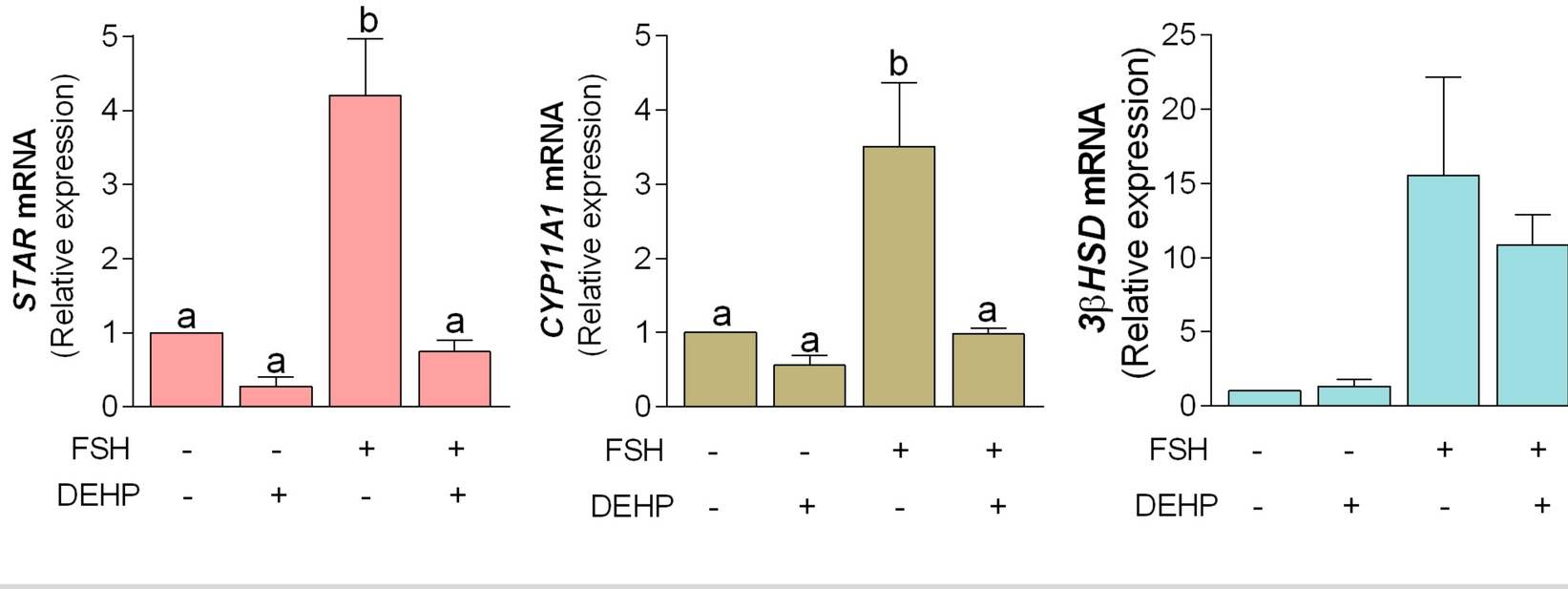
Human cumulus granulosa cells , obtained from patients undergoing *in vitro* fertilization (IVF) treated with the 25 μM DEHP and FSH or forskolin or 8-Br-cAMP for 48 h.

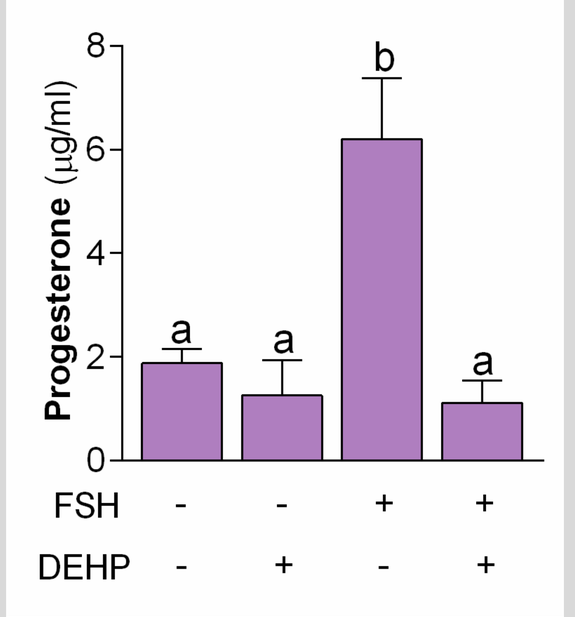


Quantitative RT-PCR- mRNA levels of *STAR*, *CYP11A1* and *HSD3β*
ELISA- levels of progesterone



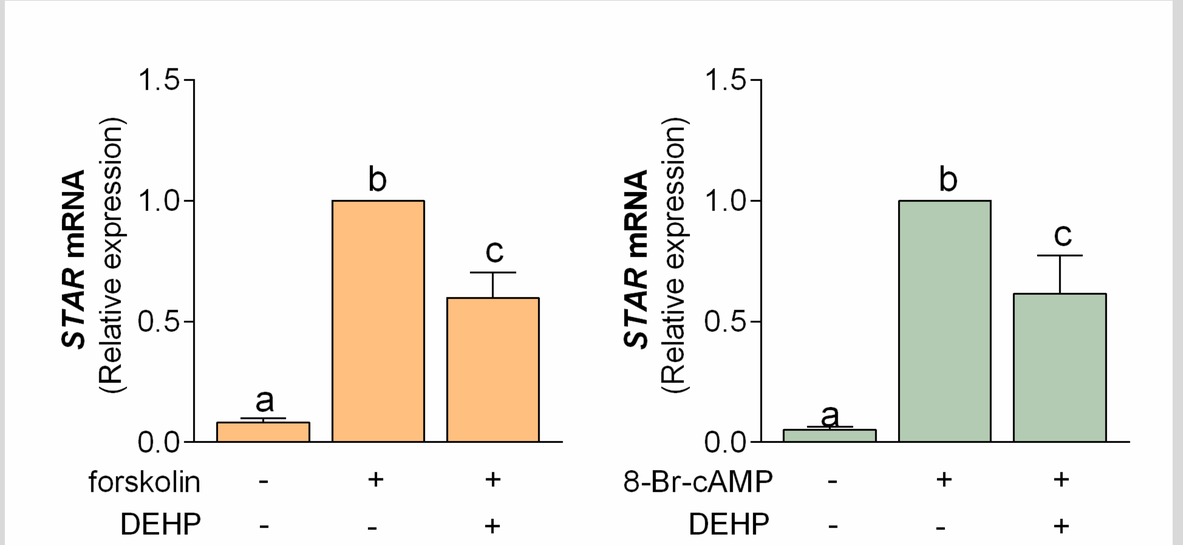
RESULTS





CONCLUSION

The results showed that DEHP did not affect the basal but decreased the FSH-stimulated progesterone production. DEHP reduced the mRNA expression of steroidogenic acute regulatory protein (*STAR*) and cholesterol side-chain cleavage enzyme (*CYP11A1*) but did not change the 3beta-hydroxysteroid dehydrogenase (*HSD3B*) gene expression**.** Furthermore, DEHP exposure reduced the forskolin- and 8-Br-cAMP-stimulated *STAR* mRNA expression in human granulosa cells. This study showed that acute exposure to DEHP decreased the FSH-stimulated progesterone synthesis by reducing the mRNA expression of the two key enzymes in the progesterone biosynthetic pathway, namely STAR and CYP11A1.



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