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# **Natriceuticals and Their Impact in Modulation of Epigenetic Effects Induced by Environmental Chemicals**

By

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**Abstract:** The transgenerational epigenetic inheritance induced by environmental contaminants in mammals has been playing important role in the inheritance of male and female reproductive dysfunction. Nutraceuticals are able to influence epigenetic mechanism and could be considered a chemopreventive agent. The present study investigated the potential effect of the *Trigonell a Foenum-graecum L (TFGL)* and *Origanum majorana L (OML)* on the epigenetic changes induced by bisphenol A (BPA) in male and female offspring. 84 pregnant female albino rats were divided into 3 groups. Group I: female rats were given orally 50 mg/kg of BPA / day during gestation and/or lactation periods, group II: *OML* was given orally to dams in a dose 250 mg /kg 3 weeks before BPA administration each as alone or in combination with BPA, and group III: *TFGL* was given orally to dams in a dose 250 mg /kg 3 weeks before BPA administration each as alone or in combination with BPA. At weaning, weaning traits were determined. At postnatal day 60 (PND 60) assayed serum testosterone, serum estradiol, serum lipid profile, and total protein, malondialdehyde (MDA) level, glutathione (GSH)level, superoxide dismutase (SOD), catalase enzyme (CAT), glutathione reductase enzyme (GR), glutathione-s- transferase (GST) and also glutathione peroxidase (GSH-Px) activities in testicular and ovarian tissues, DNA(cytosine-5)- methyltransferase 3A (DNMT3A), insulin-like 3 (INSL3) and estrogen receptor alpha (ER- $\alpha$ ) were assessed in testis and ovary by methylation specific PCR. BPA exposure resulted in decreased pregnancy

index, litter size, survival index for litters and offspring, sex ratio, AGD and AGI of male pups, testis, epididymis and ovary weights with a marked increase in male and female pups weaning body weight, AGD of female pups, BPA also decreased level of serum testosterone, estradiol and HDL – cholesterol with significant increases in the levels of serum total cholesterol, triacylglycerol, LDL- cholesterol, VLDL-cholesterol. Also BPA increased levels of MDA and decreased levels of; total protein , glutathione (GSH), and activities of hepatic antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione reductase enzyme (GR), glutathione–s-transferase (GST) and glutathione peroxidase (GSH-Px) activities in testicular and ovarian tissues. BPA caused apparent hypermethylation within DNA (cytosine-5)-methyltransferase 3A (DNMT3A), insulin-like 3 (INSL3) and estrogen receptor alpha (ER- $\alpha$ ) genes promoter region in testis of male offspring, while BPA caused marked hypomethylation within DNA (cytosine-5)-methyltransferase 3A (DNMT3A), insulin-like 3 (INSL3) and estrogen receptor alpha (ER- $\alpha$ ) genes promoter region in ovaries of female offspring. The observed antioxidant effect of *OML* and *TFGL* administration to dams could be responsible for a protective effect against epigenetic changes induced by BPA in a time- dependent manner and modulated significantly the alterations in most of the previously mentioned parameters into its normal ranges. In conclusion; the modulatory effect of *OML* and *TFGL* on transgenerational adverse epigenetic changes induced by BPA showed their potential as a protective agent against male and female fertility dysfunction.

**Keywords:** *Origanum majorana* L, *Trigonell a* *Foenum-graecum* L, Bisphenol A, Oxidative stress and antioxidant enzymes, Transgenerational epigenetics, DNA hyper/ hypo methylation, DNMT3A gene, INSL3 and ER- $\alpha$  genes.



*Dedication To*

*The Soul of My Greatest Brother  
(Hamada)*

*&*

*My Family*

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