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MALE REPRODUCTIVE HEALTH, CHEMICALS AND ENVIRONMENTAL FACTORS, A MEDITERRANEAN WORKSHOP

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International Program on Chemical Safety (IPCS)
European Environmental Agency (EEA)

IN VIVO AND IN VITRO EFFECTS OF NONYLPHENOL ETHOXYLATES ON TROUT SPERMATOGENESIS

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We investigated the effects to non-lethal concentrations of a chemical commonly discharged into the aquatic environment, (Igepal® 210, a mixture of nonylphenol mono and di-ethoxylate), on the development of spermatogenesis *in vivo*. Further we studied the effects of several nonylphenol ethoxylates on early germ cell proliferation (basal and IGF-I stimulated).

In vivo, When fish in the prepubertal stage of spermatogenesis were exposed for 21 days to NP2EO-Igepal 210, the spermatogenic process was partly inhibited (fig 1) and a 20 to 40 % reduction of the gonadosomatic index was observed 4,5 weeks post-exposure. Only the highest concentration of NP2EO induced a significant increase in blood plasma vitellogenin in male trout.

In vitro: a mixture of Sertoli and early germ cells (spermatogonia and primary spermatocytes) were cultured for 4.5 days in the presence or not of the tested molecules and with IGF-I or not. ³H-thymidine (³H-Tdr) incorporation was measured according to Loir (1999) and ¹²⁵I-IGF-I specific binding was determined according to Le Gac et al. (1996).

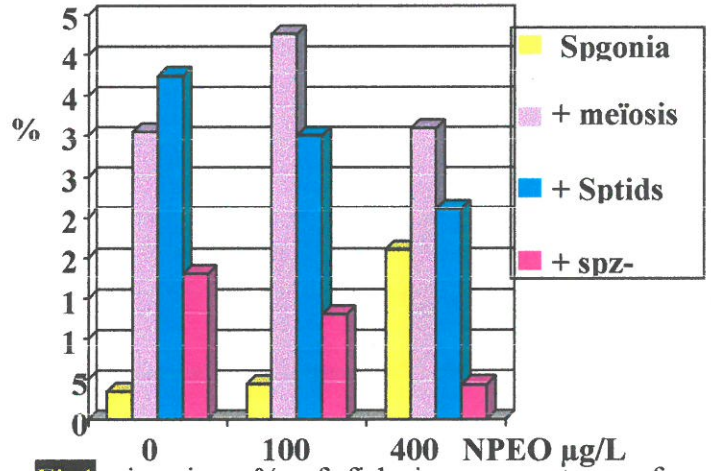


Fig1: *in vivo*, % of fish in every stage of spermatogenesis 4,5 weeks post-exposure

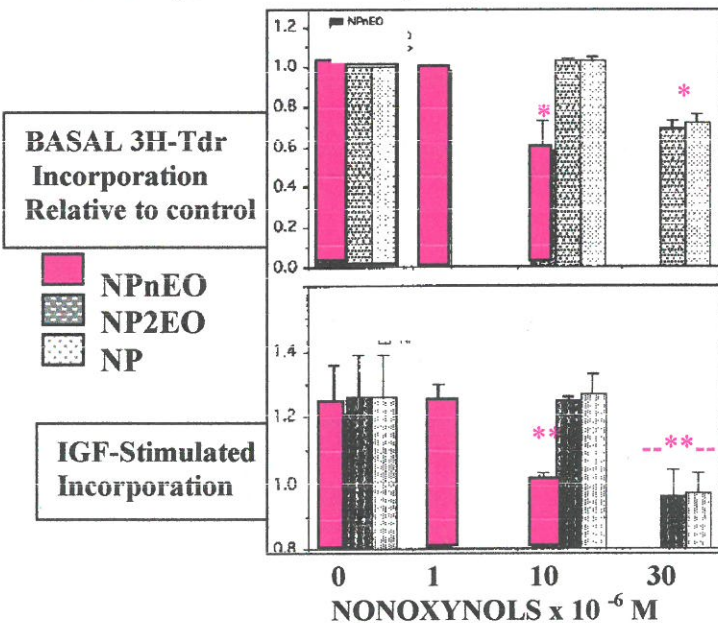


Fig2: Basal ³H-Tdr incorporation was decreased by nonylphenol polyethoxylate (NpnEO; starting at 10 µmol/L), NP2EO and NP (30 µmol/L). The presence of IGF-I (10 to 100 ng/ml) stimulated ³H-Tdr incorporation; this response to IGF-I began to decrease

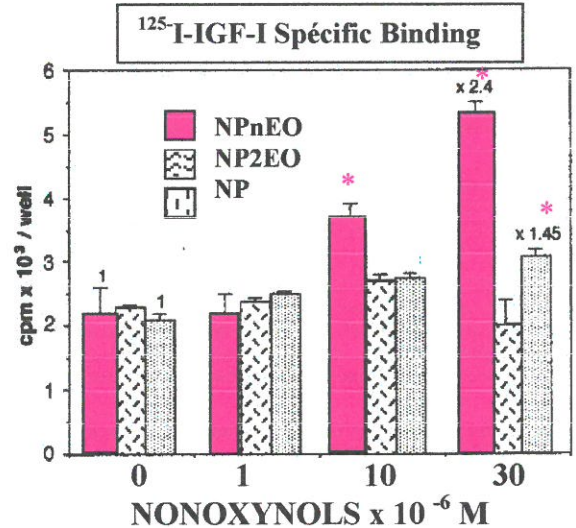


Fig3: In parallel, a dose-dependent increase of IGF receptors apparent number was induced by NP and NpnEO.

While 1 to 100 nmol/L 17α-estradiol had no effect in our *in vitro* system, Triton® X-100 acted as NPnEO on ³H-Tdr incorporation. **Beside their known E2-like disrupting effects on sex steroid production or action, these molecules could act on germ cells by disrupting cell membrane receptivity to peptide hormones like growth factors.**