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The phytoestrogen and principal isoflavone in soy, genistein, has adverse effects on reproductive physiology in rodents. Cultured mouse hepatoma Hepa-1c1c7 cells were treated with either genistein or 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) or in combination to assess the role of genistein in the process of cytochrome P450 1A1 (Cyp1a-1) induction. Treatment of Hepa-1c1c7 cultures with TCDD induced Cyp1a-1, as indicated by analysis of 7-ethoxyresorufin O-deethylase (EROD) activities. Genistein alone did not affect the activity of Cyp1a-1-specific EROD activities; in contrast, TCDD-induced EROD activities were markedly reduced in the concomitant treatment of TCDD and genistein in a dose dependent manner. Treatment with tamoxifen, an antiestrogen that acts through the estrogen receptor did not affect the suppressive effects of genistein on TCDD-induced EROD activity. TCDD-induced Cyp1a-1 mRNA levels were markedly suppressed in the concomitant treatment of TCDD and genistein consistent with EROD activity. Transient transfection assay using dioxin-response element (DRE)-linked luciferase revealed that genistein reduced transformation of the aryl hydrocarbons (Ah) receptor. These results suggest the down regulation of the Cyp1a-1 gene expression by genistein in Hepa-1c1c7 cells might be antagonism of the DRE binding potential of nuclear Ah receptor but not through estradiol receptor [This work was supported by KFDA Grant and RCPM from KOSEF].

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#### INTERNATIONAL COOPERATION STUDY FOR EVALUATION OF OECD SCREENING AND TESTING METHOD FOR ENDOCRINE DISRUPTORS

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The uterotrophic and Hershberger assays are considered as potential short term screening assays to detect the endocrine disruptors by OECD and EDSTAC. The OECD is in the process of developing these assays and validating its protocols by participating laboratories carry out the work according to each of the designed protocols. Preliminary findings suggest that these assays are robust and ready for protocol standardization and inter-laboratory validation. Therefore, the objective of this study was to provide data for the standardization of the OECD rodent uterotrophic assay (second stage) and Hershberger assay (first-stage). In the 3-day uterotrophic assay using immature female rats, neither BA and BE treatment affected mean uterus (wet and blotted) weights. However, a significant increases in mean uterine wet weights were observed in BF (775% of VC), BB (392% of VC), BC (367% of VC), BD (249% of VC), BH (232% of VC) and BG (180% of VC) groups. The changes of uterine blotted weights showed a similar pattern with uterine wet weight. Also, dose-related estrogenic effects of bisphenol-A and nonylphenol were observed. In bisphenol-A treatment groups, dose-related increases in both mean uterine wet and blotted weights were observed. Moreover, these increases were statistically significant at doses of 300 mg/kg/day and above. Nonylphenol also statistically significant increases of uterine wet and blotted weights were observed at doses of 80 mg/kg/day and above. Hershberger assay was performed utilizing immature Sprague-Dawley male rats castrated at 6 weeks of age. Testosterone propionate (0.1, 0.2, 0.4, 0.8 and 1.6 mg/kg/day) was subcutaneously (s.c.) injected for 10 days. Additionally, a pure androgen antagonist, flutamide (1, 5, and 10 mg/kg/day) was administered by oral gavage after testosterone treatment. In testosterone propionate, glans penis (GP), seminal vesicles (SV), ventral prostate (VP), levator ani muscle and bulbocavernosus muscle (LABC), and cowper's glands (CpG) weights were significantly and dose-dependently increased. Flutamide inhibited the testosterone-induced re-growth of accessory sex glands (SV, VP and Cp) and organs (GP and LABC) with dose-dependent manner. These results suggests that uterotrophic and Hershberger assays may be useful methods for detecting the endocrine disruptors with estrogenic/antiestrogenic or androgenic/antiandrogenic activity.