The screening of everyday life chemicals in validated assays targeting the pituitary–gonadal axis

H. Tinwell ⇑, S. Colombel, O. Blanck, R. Bars

Bayer SAS, 16 rue Jean-Marie Leclair, CP 106, 69266 Lyon Cedex 09, France

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abstract

Ten structurally diverse chemicals (vitamins C, B9, B6, B3, sucrose, caffeine, gingerol, xanthan gum, par- acetamol, ibuprofen) deemed intrinsic to modern life but not considered as endocrine active, were tested in vitro using the human estrogen receptor transcriptional activation (hERTa) and the H295R steroido-genesis assays. All were inactive in the hERTa assay but paracetamol, gingerol, caffeine and vitamin C affected steroidogenesis in vitro from 250, 25, 500 and 750 lM respectively. One molecule, caffeine, was further tested in rat pubertal assays at the tumorigenic dose-level and at dose-levels relevant for human consumption. In females pubertal parameters (vaginal opening, estrus cycle), ovarian weight and Fsh and prolactin transcript levels were affected. In males, plasma progesterone levels and prostate and seminal vesicle weights were affected.

Although the current regulatory focus is synthetic chemicals that can cause adverse effects on the hypo- thalamus-pituitary–gonadal axis, our data infer that the range of natural chemicals with the potential to affect this axis may be extensive and is probably overlooked. Thus, to avoid regulation of an overwhelming number of chemicals, a weight of evidence approach, combining hazard identification and characteriza- tion with exposure considerations, is needed to identify those chemicals of real regulatory concern.