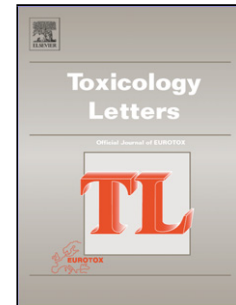


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Endocrine disrupting activities and immunomodulatory effects in lymphoblastoid cell lines of diclofenac, 4-hydroxydiclofenac and paracetamol

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Highlights

- PAR is GR agonist with direct binding activity on receptor.
- Only 4-HD metabolite display estrogenic, androgenic (in YAS assay) and thyroid hormonal activity.
- Endocrine disrupting activities of metabolite 4-HD were less potent compared to DIC, except anti-androgenic activity.
- DIC and BPA showed immunomodulatory effect.

ABSTRACT

A critical literature review reveals that knowledge of side effects of pharmaceuticals diclofenac and paracetamol is extremely important because of their widespread use and occurrence in the environment. In order to delineate whether these compounds have endocrine activity and influence on the immune system, we assessed the potential endocrine disrupting and immunomodulatory activities of: diclofenac (DIC), its metabolite 4-hydroxydiclofenac (4-HD) and paracetamol (PAR). Herein, we report on their impact on estrogen receptor (ER), androgen receptor (AR), glucocorticoid receptor (GR) and thyroid hormone receptor (TR). The endocrine disrupting effects were assessed *in vitro* in MDA-kb2 and GH3.TRE-Luc cell lines and by the XenoScreen YES/YAS assay. Moreover, binding affinity to nuclear receptors (GR and AR) was also measured. Immunomodulatory properties of the compounds were evaluated in lymphoblastoid cell lines. All the tested compounds showed endocrine disrupting and immunomodulatory activities. The results revealed that both DIC and its metabolite 4-HD exhibited significant estrogenic, anti-androgenic (in YAS assay), (anti)-androgenic, (anti)-

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