EFFECTS OF PCB101, PCB118, PCB138 AND PCB153 ALONE AND IN MIXTURE IN MCF-7 BREAST CANCER CELLS: POSSIBLE MECHANISM OF ACTION

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Polychlorinated biphenyls (PCBs) are ubiquitous environmental persistent contaminants giving rise to potential health hazard. Depending on the position and number of chlorine substitutions, different classes of PCB congeners elicit a complex spectrum of biological and toxic responses in a number of in vivo and in vitro models. Moreover, some PCBs have been shown to have potential estrogenic and antiestrogenic effects.
In the present study we have analysed the potential estrogenic effect in MCF-7 cells of four very biologically relevant PCB congeners alone and in mixture; PCB 101 (2,2',4,5,5'-pentachlorobiphenyl), PCB 118 (2,3',4,4',5-pentachlorobiphenyl), PCB 138 (2,2',4,4',5,5'-hexachlorobiphenyl) and PCB 153 (2,2',3,4',5,5'-heptachlorobiphenyl). The mixture of four PCBs was tested at seven different concentration choosen on the basis of their real ratio of dose in some food types. The ability of these PCBs alone and in mixture to induce cell proliferation and the level of estrogen-regulated protein pS2 was studied using the human MCF-7 breast cancer cells.
In MCF-7 cells, PCB 153 35 μM stimulates cell proliferation from 48 h up to 6th day, while PCB 118 40 μM only at 48 h. No effect were observed after treatment with PCB 101 45 μM and PCB 138 10 μM for 6 days. The treatment with different mixture concentrations causes a significant decrease of cell proliferation at different time. No variation of pS2 level was observed after treatment with the different PCBs alone and in mixture.
In exploring the mechanism mediating these events and its timing, we found that PCB 153 was able to induced mitogen-activated protein kinase (MAPK) ERK1/2 at 4, 8 and 12 h, while the antiproliferative effect seems to be mediated by an apoptotic action beginning at 12 and ending at 48 h.
The data demonstrated that these PCBs alone and in mixture have not estrogenic effect in MCF-7 cell, while PCB 153 and PCB 118 induce a mitogenic effect, ERK1/2 mediated. On the contrary, the mixture of all PCBs induces an antiproliferative effect mainly at higher concentrations ascribed to an apoptotic phenomenon.