

Structural binding interaction of polybrominated diphenyl ethers (PBDEs) with thyroxine binding globulin: Insights into thyroid signaling disruption

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Polybrominated diphenyl ethers (PBDEs) represent an important class of halogenated flame retardants incorporated into a variety of consumer products to slowdown the spread of fire and mitigate the damage to property and human life. They have widespread environmental presence attributed to their leach out from consumer products and persistent nature making them resistant to degradation. Multiple studies have highlighted the structural resemblance between PBDEs and thyroid hormones, allowing them to mimic thyroid hormone activity and potentially disrupt its function. Therefore, it becomes pertinent to investigate and gather more data on PBDE induced thyroid dysregulation and associated toxicological effects in humans. Thyroxine-binding globulin (TBG) regulates thyroid hormone metabolism and its distribution in body making it vital for controlling thyroid hormone homeostasis. The objective of this study was to investigate the molecular interactions of commonly detected PBDEs, BDE-100 and BDE-209 with in the TBG ligand binding pocket. These ligands underwent Schrödinger's induced fit docking (IFD) along with structural binding analysis, which included molecular interaction evaluation and binding energy calculation. The analysis demonstrated that all the ligands were strongly bound within the TBG pocket, with a high degree of similarity in the TBG interacting residues between the specified PBDE ligands and the native TBG ligand, thyroxine. The calculated binding energy values for BDE-209 were higher than that of TBG native ligand, while BDE-100 values were somewhat lower but not significantly so. In conclusion, the results indicated that BDE-209 is more effective than BDE-100 in inhibiting the binding of thyroid hormones to TBG, though both PBDEs possess this ability. As a result, this could disrupt the circulatory transport of thyroid hormones and their availability at target sites, potentially causing thyroid dysregulation.

Keywords: Endocrine disruption, Polybrominated diphenyl ethers, Thyroid dysregulation, Structural characterisation