

## Role of polybrominated diphenyl ethers in thyroid hormone transport disruption

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Polybrominated diphenyl ethers (PBDEs) are extensively used brominated flame retardants and are considered endocrine-disrupting chemicals (EDCs) due to their structural similarity with thyroid hormones. The growing concerns regarding the potential endocrine-disrupting effects of polybrominated diphenyl ethers (PBDEs) on human health have prompted a need for detailed investigations into their molecular interactions with critical proteins involved in hormone transport and regulation. Thyroxine-binding globulin (TBG) plays a pivotal role in the transport and regulation of thyroid hormones, which are essential for numerous physiological processes, including metabolism, growth, and development. The aim of this study was to investigate the structural interactions of commonly detected four PBDEs ligands, BDE-28, BDE-85, BDE-154 and BDE-183 against thyroxine-binding globulin (TBG). The indicated four PBDEs ligands were subjected to structural binding characterization against the TBG ligand binding pocket using Schrodinger's induced fit docking. Further, the structural analysis of TBG-ligand complexes including the molecular interaction and binding energy estimation was also performed. The results indicated the stable and tight binding of all four PBDE ligands in TBG ligand binding pocket and high percentage of commonality in interacting amino acid residues with that of TBG native ligand, thyroxine (T4). Furthermore, the estimated binding energy values for BDE-154 and BDE-183 were very close to each other and approximately same as that of T4. However, the predicted values for the remaining two ligands, BDE-28 and BDE-85 were lower compared to the estimated values of T4. In conclusion, on a preliminary basis, the results of our study suggested that the indicated PBDEs, especially BDE-154 and BDE-183, have the potential to interfere in the binding of thyroid hormones to TBG. This interference disrupts the circulatory transport of thyroid hormones which might have implications in thyroid associated health outcomes.

**Keywords:** Flame retardants, Polybrominated diphenyl ethers, Structural studies, Thyroid hormone transport, Endocrine disruption