With industrialization, the production of chemicals and their introduction into the environment has increased massively. Some of these chemicals act as endocrine disruptors (EDs) as they disturb endogenous hormone signalling pathways and alter the normal functioning of the endocrine system of both humans and wildlife. They either mimic or interfere with the action of endogenous hormones like thyroid hormones (THs), and other chemicals of the endocrine system. Group of these compounds include polychlorinated biphenyls (PCBs) and their hydroxylated metabolites (OH-PCBs). Their most important chemical property is their good lipid solubility and ability to pass through biological membranes, which means that they can easily accumulate in an adipose tissue, and when released from them, often after several years, may cause serious diseases. These compounds show several metabolic and toxic activities including mutagenic, immunotoxic and carcinogenic effects. The effect of PCBs and OH-PCBs on thyroid hormone metabolism is not fully examined. Due to the similar chemical structure to iodothyronine molecules, these compounds may modulate or disturb the functions of many organs, as well as endocrine glands, including the thyroid gland. Moreover, the molecular mechanism of these compound actions in thyroid cells and hepatocytes has not been elucidated.

Therefore, the aim of this research is to determine and compare the effect of PCB126 (planar PCB congener) and PCB 153 (non-planar congener) and their hydroxylated metabolites (4'-OH-PCB126 and 4-OH-PCB153, respectively) on synthesis and metabolism of iodothyronine in the thyroid gland and liver of the chicken (*Gallus domesticus*) - a model organism in this type of research.

It is planned to carry out *in vitro* experiments that will answer the following questions:

Whether PCBs and OH-PCBs:

- affect the secretion of iodothyronine from explants of thyroid gland and liver in hens?
- affect the TSH-stimulated secretion of T_4 and T_3 from the chicken thyroid gland?
- as well as their combinations with TSH (in respect to the thyroid gland) or DEX (in respect to the liver) may influence deiodinases concentrations (D1 and D3) - enzymes involved iodothyronines metabolism?
- affect mRNA expression of the genes encoding:
    - proteins and enzymes involved in the TH synthesis and metabolism,
    - TH transmembrane transporters in thyroid and liver cells,
    - thyroid stimulating hormone receptors (TSH-R) in the thyroid gland and nuclear TH receptors (TRs) in the liver?

Although environmental concentrations of PCB and OH-PCB have been gradually decreasing since 2001 (as a result of the Stockholm Convention on Persistent Organic Pollutants) they are still detected at high levels in human and animal tissues. Despite extensive knowledge concerning effects of PCBs on many biological processes, there are still scarce data regarding the impact of OH-PCBs, whose concentrations in the environment are still increasing, on TH synthesis and secretion and iodothyronine metabolism in peripheral tissues (such as the liver) responsible for maintaining a physiological level of T_3 in blood. Moreover, molecular mechanisms of these compounds in thyroid cells and hepatocytes have not been elucidated. The research project, due to its innovativeness and high cognitive value, will not only make a significant contribution to expanding the knowledge on the impact of PCBs and their metabolites on previously mentioned processes, but they may also be useful for human medicine.