

1. PHD PROJECT DESCRIPTION (4000 characters max., including the aims and work plan, all in English)

Project title:

1.1. Project goals

The main objective of the proposed studies will be to provide the largest possible amount of reliable data that will allow for a complete and reliable exposure assessment of patients with hypothyroidism to the effects of selected xenoestrogens. The research carried out in this area will cover three main fields: 1) the first and overarching goal is related to the development of new analytical tools enabling the isolation of selected compounds from a biological matrix (urine, plasma, serum), 2) development of various analytical methods and procedures for the determination of selected substances by liquid chromatography with spectrophotometry, spectrofluorimetry and mass spectrometry. The developed analytical tools will be used to assess the degree of patients' exposure to environmental pollution with selected xenoestrogens and to quantify the processes related to the assessment of their penetration into the body and a qualitative description of the observed biological effects.

1.2. Outline

Hypothyroidism is a clinical syndrome caused by a deficiency of thyroid hormones or the result of a decreased sensitivity of tissues to these hormones. Hypothyroidism affects 1 - 6% of the population. It is 4-5 times more common in women and its frequency increases with age. In Poland, the most common cause of hypothyroidism is damage to the thyroid gland caused by autoimmune inflammation [1]. In recent years, more and more attention has been paid to foreign compounds present in the environment (xenoestrogens) and having estrogen-like properties, which may play a significant role in the etiopathogenesis of hypothyroidism. There is great interest in the potential relationship of thyroid dysfunction with the accumulation of toxic metals (e.g. lead, chromium (VI), cadmium, arsenic, mercury, nickel) or the deficiency of micronutrients (e.g. copper, manganese, etc.). This is only a small fraction of compounds considered as potentially disrupting the proper functioning of the endocrine system [2]. Despite the several years of research, it was not possible to draw clear conclusions concerning the correlation of the concentrations of some elements and compounds disrupting endocrine functions (including parabens, bisphenols, triclosan) with the occurrence of hypothyroidism and the associated increased process of autoimmunity [3]. Therefore, it is justified to continue research in this area. The developed analytical tools in the form of selective sorbents will allow for the quantitative isolation of selected xenoestrogens. Additionally the improved and validated analytical procedures using liquid chromatography with various detectors will enable obtaining reliable results. The studies will be conducted in adult patients (18-50 years old) with primary hypothyroidism of various etiologies, with particular emphasis on autoimmune thyroiditis. The obtained results will allow to broaden the knowledge and attempt to explain the constantly increasing incidence of the above diseases, which in turn may translate into the implementation of preventive measures aimed at reducing the risk of exposure to endocrine active compounds.

1.3. Work plan

- development of the synthesis of selective sorbents and their physicochemical characteristics for the isolation of selected xenoestrogens (including parabens) from plasma and urine,
- develop a method for the preparation of samples using the QuEChERS method and/or solid phase extraction for the isolation of triclosan,
- providing a novel analytical approach to the rapid determination of the toxic metal ions by selective sensors to perform the complete physico-chemical characterization,
- optimization of elution conditions in liquid chromatography and selection of detector parameters for selected compounds,
- statistical analysis, molecular modeling, processing and interpretation of the obtained results

1.4. Literature

1. Koeppe ES, Ferguson KK, Colacino JA, Meeker JD. *Sci Total Environ.* 2013; 445-446:299-305. doi:10.1016/j.scitotenv.2012.12.052]
2. Street ME, Angelini S, Bernasconi S, et al., *Int J Mol Sci.* 2018;19(6):1647.
3. Liao Ch, Chen L, Kannan K, *Environ Int.* 2013 Jul;57-58:68-74. doi: 10.1016/j.envint.2013.04.001

1.5. Required initial knowledge and skills of the PhD candidate

The PhD candidate should be experienced in the preparation of biological samples and liquid chromatography with the use of various detection methods. Additionally, knowledge of new solutions will be assessed for different sample preparation methods. An additional advantage is analytical thinking skills and effective problem solving, independence, responsibility and the willingness to develop and learn new instrumental techniques.

1.6. Expected development of the PhD candidate's knowledge and skills

PhD student in the course of the proposed research implementation will gain knowledge and skills in the field of analytical chemistry and synthesis of new materials sorption. The candidate will acquire specialist knowledge in identification of selected xenoestrogens, the synthesis of sorbents and their physicochemical characteristics. The PhD student will be able to develop new, previously unknown procedures and analytical methods for the determination and identification of selected substances with the use of ultra-high-performance liquid chromatography in combination with various detectors. During the studies, the student will be able to present the obtained data through of publications, posters and oral presentations at national and international conferences.