Reg. No: 2021/41/N/NZ7/00313; Principal Investigator: mgr Andrzej Patyra

Wood from pine family (Pinaceae) native to Poland as a potent source of pharmacologically active lignans

Almost 70% of the area of Polish forests is occupied by trees belonging to one family – the pine family (lat. *Pinaceae*). Although we can include even 11 genera and 230 species, in Poland we will meet relatively few of them. These are mainly conifers such as Norway spruce, Scots pine, European larch, Norway fir and several other species that are much less common. Their economic importance is rather high – wood of these trees is used to make paper and furniture.

With current technological solutions logs and other wood products brought to sawmills are almost totally processed, leaving little to no waste. However, it is still not always the case. According to experts, low technological level of a large part of Polish industrial plants, the lack of financial resources for proper waste management, as well as the low level of public awareness are the reasons for the generation of substantial amounts of waste – among them wood knots and branch wood. Their high quality and solid structure could bring them many applications, yet they are mostly used to generate energy (as a biofuel). It is worth noting, however, that coniferous wood, in particular knots or branches rich in them, may be a source of active compounds with potential therapeutic application.

Among compounds found so far in wood of the species of pine family, lignans, seems to be of particular interest. Many of these compounds have already proven antioxidant activity, and some reports also show their antidiabetic activity. In this context, lignans are likely good candidates to ameliorate insulin secretion since several of these antioxidant compounds are now widely regarded as pharmacological agents that can possibly engage in biochemical pathways in pancreas.

Type 2 diabetes mellitus is a disease that associates inappropriate tissue response to insulin and dysfunction of pancreas. Based on current understanding of the pathophysiology of this disease, multiple antidiabetic therapies have been developed with the aim of improving blood sugar control and slowing disease progression. Nevertheless, they have limited effectiveness and numerous side effects (i.e. digestive disorders for metformin and hypoglycemia for sulfonylureas).

One possible approach targeting pancreatic beta cell (cells responsible for insulin secretion) is the use of compounds that improve insulin secretion dependent on blood sugar levels; a safer strategy to help achieve glycemic goals due to lower risk of hypoglycemia (low blood sugar level). The development of such lead molecules is still an active area of research in order to provide more therapeutic options in the future as the number of type 2 diabetic patients keeps growing.

The **aim** of this project is to analyze branch wood extractives of the pine family species native to Poland in search of a new source of potentially active compounds and thus finding an application for wood industry waste materials. Previous biological activity reports of lignans in terms of antidiabetic effect, as well as reports on high lignan content of conifer wood and our preliminary data led to the **hypothesis** that branch wood from the pine family species could be a rich source of novel antihyperglycemic agents.

To verify this hypothesis, we will conduct research into the phytochemical composition of branch wood using chromatographic and spectrometric methods for selected trees. Isolated compounds will be investigated on cell models such as insulinoma cell line (INS-1) and isolated pancreatic islets to assess their impact of insulin levels as well as their antioxidant, and protective properties.

This project will shed light on how lignans show their pharmacological effects and how they improve insulin secretion. It may be the first step in the design of new natural or semi-synthetic compounds that improve the function of the pancreas for the prevention and / or treatment of diabetes. It will also allow us to examine the content of Polish tree species from the pine family and find a potential application for waste from the wood industry.