The use of iodoquinolines for biostimulation and biofortification of selected vegetables in iodine and investigation of their anticancer properties in the *in vitro* breast cancer model

The aim of the project are 1) Comparison of effectiveness between *de novo* synthetized iodoquinolines in biostimulation and biofortification in iodine of selected vegetables (kale and early potato; **2)** Assessment of the minerals management of biofortified-plants and the metabolism of iodoquinolines in plants; **3)** Evaluation of the impact of selected culinary and technological processes on the iodine content and selected pro-health parameters of iodoquinoline-biofortified vegetables; **4)** Determination of cytotoxic activity of *de novo* synthetized iodoquinolines and iodoquinoline-biofortified vegetable extracts; **5)** *In vitro* investigation of potential anticancer effect of iodoquinoline-biofortified vegetable extracts on breast cancer cells; **6)** Assessment of the iodine bioavailability from iodoquinoline-biofortified vegetables in Wistar rats and analysis of chosen biochemical parameters of thyroid gland-regulated processes.

Project hypothesis (based on the preliminary results) is that 1) iodine bioavailability and uptake in plants largely depends on its chemical form; Iodine applied to plants in the organic form of iodoquinolines will be not only equally but more efficiently absorbed and accumulated by plants compared to the inorganic, mineral forms; **2)** Iodoquinolines will undergo conversion in plants in different metabolic pathways than the mineral iodine forms (iodides and iodates); as a result, secondary iodoquinoline metabolites will be generated; **3)** iodoquinolines themselves have anti-cancer properties; thus the presence of secondary metabolites will strengthened the anti-cancer activity of biofortified vegetables. **4)** The presence of a nitrogen atom in the pyridine ring of iodoquinolines will have a biostimulative effect on plants; thus, significantly increasing the crops.

Taken together, Grant's hypothesis assumes to achieve the combined effect of biostimulation and biofortification of tested vegetables with gained anticancer potential. The problem of iodine deficiency is still on-going and very common. The associated negative health effects are a heavy burden to the public health system. According to the recent WHO recommendations, current high salt intake per person should be reduced to 5g NaCl day; thus, present iodine prophylaxis, involving the use of iodized table salt, will become insufficient. On the other hand, excessive consumption of salt is associated with an increased risk of cardiovascular disease. Thus, biofortification of vegetables with iodine may become an effective and a low-cost strategy to prevent iodine deficiencies and a safe alternative to iodination of table salt. Such an approach is currently recommended by the WHO and has been recently also emphasized during the 1st International World Iodine Association (WIA) Conference "Iodine in food systems and health" (Pisa, Italy, 2017).

Iodine biofortified-vegetables can become a good source of this micronutrient due of their relatively high recommended dietary consumption; without the risk of its excessive intake.

Over the last decade research was mainly focused on the optimization of agronomical methods of biofortification of plants with mineral forms of iodine (KI or KIO_3). However; their effectiveness is limited due to the strong sorption of inorganic iodine forms into soil organic matter and transformations caused by reactions with humic acid, leading to iodine volatilization and its release to the atmosphere. In addition, iodine has been also found released from the plant as a methyl iodide (CH3I). To further improve the bioaccumulation of iodine in selected vegetables we propose the use of iodoquinolines as organic iodo-compounds.

Iodoquinolines represent a small fraction of all quinoline derivatives, which demonstrate a variety of medical properties, including anti-microbial, antifungal, antiviral, anti-inflammatory and antitumor. The broad spectrum of biological and biochemical activities of quinolines is facilitated by their synthetic versatility useful when synthesizing new derivates (e.g. iodoquinolines). Available literature is very limited on the effect of iodoquinolines on cancer cells. The investigation of the molecular mechanisms behind the reduction of cancer cells viability is also an innovative element of proposed project. It should be emphasized that both quinoline and iodine have a documented therapeutic anticancer effect. In addition it should be emphasized that quinoline derivatives have antiviral activity. Wide range of collected data on the effects of novel synthesed iodoquinolines will have a high scientific value and will potentially inspire new directions for further studies e.g. regarding to COVID-19.