Great efforts in searching of novel candidates for cancer disease therapy are fully justified in the context of major problem facing current healthcare. Malignant neoplasms are the second cause of death in United States and Europe. Despite decrease in overall death and incidence rate observed in recent years due to advancement in medical treatments, the long-term prognoses does not reduce concerns, as incidence rate is expected to rise approximately 70% by the year 2035 due to demographic effect. More detailed insight into the most recent epidemiologic data shows that among leading types of malignant neoplasms those developed from lung and breast tissues are most frequent being also a leading cause of cancer mortality. Meanwhile, analysis of recent trends in clinical practice of cancer treatment demonstrates significant shift in prescriptions and financial expenditures from conventional chemotherapeutics to novel targeted drugs as a more specific, effective and inducing less side effects alternative. Simultaneously we observe rising concerns about limitations of targeted therapy and its economical toxicity what creates even bigger anticipation for new potential therapeutics.

Biotechnological approaches harnessed for production of pharmaceutically valuable compounds fulfil anticipation for novel methods in drug research, allowing for exploitation of unique biosynthetic abilities of living organisms. One of the possibilities is usage of plant biomass for novel compounds production. Serving humanity for millennia as a natural therapeutics, plants are constantly the significant feedstock in current pharmaceutical industry and source of leads in drug development research.

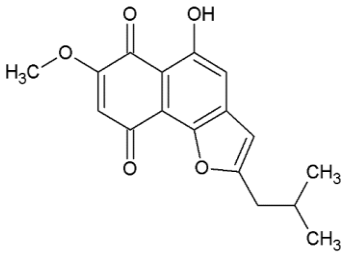
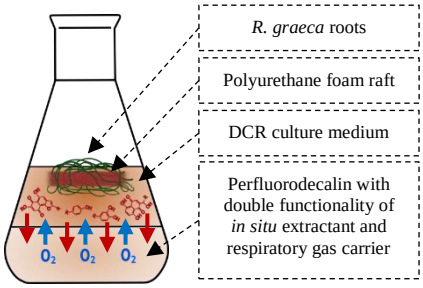


Figure 1. Chemical structure of rinderol

Two complementary purposes will be fulfilled in this project. The first aim is application of bioengineering techniques that will allow to produce substantial amounts of newly identified plant metabolite belonging to the group of naphthoquinone derivatives named **rinderol** (2-methoxy-5O, 6-(isohex-1-ene-1,2-diyl)-5,8-dihydroxynaphthalene-1,4-dione). The second aim of current project is the elucidation of the molecular mechanism underlaying its anticancer properties. Rinderol was identified and selected for the investigation among metabolites found in phytochemical profile of ***Rindera graeca*** (*Boraginaceae*) roots cultured *in vitro*, on the basis of distinguishing, micromolar cytotoxicity against various cancer cell lines.



First technique that will be applied for potential enhancement of rinderol biosynthesis in *R. graeca* roots is *in situ* extraction with perfluorodecalin which allows for accumulation of produced secondary metabolites in additional liquid phase supplemented into the culture system. Decrease in bioactive metabolites concentration reduces toxicity of culture medium, as well as biosynthesis feedback inhibition. Second modification, roots immobilization on polyurethane foam, provides microenvironment favorable for secondary metabolites production. Our preliminary research indicates on synergistic effect of both techniques after simultaneous application.

In the second, main stage of planned research, the molecular mechanism of rinderol anticancer activity will be elucidated against selected cell lines of lung an breast cancer. According to most recent knowledge, selected for the investigation rinderol structure based on the furanonaphthoquinone moiety may be responsible for enhanced anticancer potency. However, to our best knowledge rinderol unique structure has not been yet examined. Detailed evaluation of anticancer potential and effect of rinderol against key features of cancer cells is going to be performed in presented project and compared with activity of doxorubicin – clinically established drug in cancer therapy. Planned experiments encompasses determination of rinderol cytotoxicity, induced cell death type, alterations in cell signaling pathways deregulated in cancer cells, activity of transcription factors responsible for metabolism, proliferation and invasiveness of malignant cells. Investigated will be also effect of rinderol on mitochondrial membrane potential, level of intracellular reactive oxygen species, activity and expression of pyruvate kinases which are key elements regulating metabolism of cancer cells (Warburg effect).

Results obtained from both stages of planned research will allow for determination of selected bioengineering techniques effectivity in rinderol biosynthesis enhancement and for evaluation of its biological activity mechanism potential to the role of anticancer drug.