

POPULAR SCIENCE SUMMARY

Rapid technological advancement in the field of phytochemical analysis and phytopharmacology, that took place in the last decade, makes it possible to overcome the common barriers in identification of biologically active plant constituents and molecular mechanisms of their activity. The results of extended metabolomic studies of plant materials and related pharmacological and statistical analyses have become a starting point for the development of new, effective and safe medicines based on standardized plant extracts. Along with the progress in the research concerning plant substances used in official medicine, exceptionally expansible is the scientific trend aiming to identify new sources of natural drug and to reclaim for medical practice partly forgotten traditional herbal medicines.

In an attempt to follow this trend, the presented project specifically focuses on American wintergreen (*Gaultheria procumbens*) – widely used by Native Americans medicinal plant with poorly recognized chemical composition and still not fully explained mechanism of biological activity. The most commonly used plant tissue of *G. procumbens* are leaves, traditionally valued as anti-inflammatory, antipyretic and analgesic agent as well as a source of essential oil of wintergreen type. Active constituents of *G. procumbens* leaves are believed to be salicylates, primarily methyl salicylate, constituting 95% of essential oil, and its glycosidic precursor – gaultherin – present mainly in fresh plant material. This conception seems to underrate the impact of other polyphenolic compounds, which may be equal or even higher than that of salicylates, especially considering the instability of gaultherin and the volatility of essential oil as well as the fact, that traditional medicine uses mostly dried material often in form of infusions. Similar findings were described for willow bark (*Salicis cortex*, Ph. Eur. 8th, FP X), where other polyphenols present alongside salicylates were found to have significant influence on anti-inflammatory, analgesic and antipyretic activity of the plant material. However, the available data concerning polyphenols other than salicylates in the leaves of *G. procumbens* are only fragmentary and do not allow for verification of this hypothesis. The plausibility of the hypothesis is in turn supported by the investigation into the aerial parts of *G. yunnanensis* Rehder, that demonstrated significant correlation between anti-inflammatory and antioxidant activity typical of polyphenols. At the same time, the research carried out lately by the Project Manager, concerning the qualitative and quantitative profile and biological activity of *G. procumbens* leaves, gave promising results raising the possibility of wider application of investigated species in the treatment and prophylaxis.

Thus, the aim of the project is to verify the hypothesis about the value of various *G. procumbens* plant tissues (leaves, stems and fruits) as sources of potentially new or rare biologically active compounds with anti-inflammatory and antioxidant activity. The investigations will be carried out on dry extracts obtained from aforementioned plant materials. The qualitative and quantitative profile of the extracts will be studied using spectrophotometric and chromatographic (i.a. UHPLC-PDA-HR-ESI-QTOF-MS³, HPLC-PDA) methods. In the next stage the extracts with the highest content of active compounds will be selected for further analyses, i.e. isolation studies and biological activity tests. Isolation of active constituents will be performed using preparative HPLC, flash and open column chromatography. The extracts and the isolated compounds after full structural identification by spectroscopic and chemical methods will be evaluated in terms of their biological activity. To this end, the analytes will be subjected to *in vitro* tests of antioxidant (DPPH, FRAP, inhibition of linoleic acid inhibition, scavenging of superoxide anion and hydroxyl radicals, and reduction of hydrogen peroxide tests) and anti-inflammatory (hyaluronidase, lipoyxygenase and cyclooxygenase inhibition tests) activity. Subsequently, their cytotoxicity, cellular antioxidant activity in oxidative burst model on human neutrophils and the influence on pro-inflammatory functions of neutrophils in release tests of elastase, matrix metalloproteinase and selected pro-inflammatory cytokines will be studied. Finally the statistical analyses, including correlation tests, will be carried out in order to establish the relevance of specific analytes and groups of analytes for investigated activity.

The results will allow for comprehensive characterization of the *G. procumbens* polyphenolic profile, assessment of the value of leaves, stems, fruits of the title taxon as sources of biologically active compounds as well as will provide rational justification of their traditional phytotherapeutical application. The results could also constitute a starting point for further phytochemical, pharmacological and toxicological studies required to verify the applicability of the investigated plant extracts as a reasonable alternative for currently available pharmaceuticals.