The intraspecific variance of *Hypericum perforatum* - a metabolomics approach

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The genus *Hypericum* comprises around 450 species, of which *Hypericum perforatum*, commonly St. John's Wort, is the best known. Extracts of the aerial parts of this herb are prescribed to treat mild to moderate depressions, but recently also anti-microbial, anti-inflammatory, and anti-Alzheimer effects were reported. For these reasons it is among the ten best-selling herbal products in Europe and the USA. The medicinal effects of the extracts highly depend on the chemical composition, which is genetically predetermined and strongly influenced by the environment. Major active constituents are phloroglucinols (hyperforin), naphthodianthrones (hypericin), and flavonoids. The economic importance and the chemical diversity of the secondary metabolites make *H. perforatum* an interesting target of phytochemical investigations.

In this study comparative metabolite profiles of 93 *H. perforatum* accessions with different genetic backgrounds were investigated to estimate the intraspecific diversity. The genotypes were cultivated under identical conditions and harvested during the flowering period to exclude the impact of environmental factors. Flowers and leaves were sampled separately and were subsequently chemically characterized by UHPLC-ESI-HRMS. The untargeted metabolite profiling enables the simultaneous detection of hundreds of metabolites. Using multivariate data analysis the chemical diversity of the extracts was evaluated. The genotypes differ especially in the content of the phloroglucinol hyperforin. One genotype was found to not contain this active compound and showed less prenylated hyperforin precursors. Additionally, the substitution pattern of quercetin derivatives varied widely between all genotypes. The examination of the required marker compounds of *Hyperici herba* revealed that more than 20% of the extracts did not fulfill the specification of the European pharmacopeia.

This untargeted metabolomics concept combined with multivariate data analysis enables the investigation of the natural product diversity within the species, elucidation of biosynthetic pathways, and the selection of genotypes with a suitable compound composition according to the proposed pharmacological application of the economically important species.

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