Abstract

Over the past few decades, global prevalence of type 2 diabetes (T2D) has increased dramatically worldwide, causing large economic burdens for the health system of many countries. T2D is characterized by insulin resistance and associated with severe and life threatening complications such as high blood pressure, blindness, kidney failure, lower limb amputation, heart disease and stroke. Vietnam is a tropical country with thousands of plant species and many of them have been used traditionally for the treatment of T2D. These plants are of great potential in antidiabetic drug discovery but only a few has been pharmacological evaluated. Therefore, the overall objective of this study is to investigate the ability to control hyperglycemia of selected Vietnamese medicinal plants as well as identify their bioactive components. This will help to develop functional foods or lead compounds for use against T2D.

In the first project, 18 Vietnamese medicinal plants that have been used in folk medicine to treat T2D were investigated for inhibition of $\alpha$-glucosidase and $\alpha$-amylase, two key enzymes involved in serum glucose regulation. In order to accelerate the identification process of antidiabetic principles directly from the crude extract, high-resolution $\alpha$-glucosidase and $\alpha$-amylase profiling which enabled pinpointing of major and minor peaks correlated with inhibitory activity were applied. The project resulted in 11 ethanol and water extracts that significantly suppressed $\alpha$-glucosidase and $\alpha$-amylase, suggesting that Vietnamese plants are sources of carbohydrate-hydrolyzing enzyme inhibitors. Corilagin, repandusinic acid A, and mallotinin were potent $\alpha$-glucosidase inhibitors contributing significantly to the inhibitory effect observed for the water extracts of *Phyllanthus amarus* and *Phyllanthus urinaria*. In the second project, *Garcinia oblongifolia* was screened for inhibitory activity against the $\alpha$-glucosidase and protein tyrosine phosphatase 1B (PTP1B). This led to the subsequent isolation of 11 bioactive xanthones; three of which, namely oblongixanthone F-H, are new compounds. In the last project, the 18 medicinal plants continued to be evaluated for PTP1B inhibitory activity. The combined use of high-resolution PTP1B profiling and high performance liquid chromatography–high-resolution mass spectrometry–solid phase extraction–nuclear magnetic resonance, *i.e.*, HPLC-HRMS-SPE-NMR considerably accelerated the identification and structural characterization of isoderrone, derrone and alpinumisoflavone that responsible for the inhibitory activity from *Ficus racemosa*. 
In conclusion, Vietnamese medicinal plants are as promising sources for antidiabetic drug leads. The study also demonstrated the potential of high-resolution bioactivity profiling, and its further coupling with HPLC-HRMS-SPE-NMR, in drug discovery-oriented natural product research.