Abstract

Natural products have made a great impact in the history of drug discovery, and valuable information has been extracted from the discovery of naturally occurring bioactive compounds. In the battle against diseases such as type-2 diabetes and cancer, several prescribed drugs are derived from natural sources, and new bioactive compounds keep emerging, showing the great potential of natural products in drug discovery. Cancer and diabetes are both diseases affecting millions of people, with cancer being one of the deadliest diseases in the world. The development of multidrug resistance (MDR) has further challenged successful cancer treatment, and new anti-cancer and MDR reversing agents are highly desired in the battle against cancer. The prevalence of type-2 diabetes keeps increasing, and so does the associated health-care expenditures, emphasizing the need for a successful management of the disease and prevention of its associated complications.

Two of the projects in this thesis aimed at investigating potential effects of species of the Australian desert plant *Eremophila* on antidiabetic drug targets and cytotoxicity towards colon cancer cell lines together with synergistic effects with SN-38 on SN-38 resistant cancer cells, respectively. The crude leaf resin extract of *E. glabra* exhibited activity against both protein tyrosine phosphatase 1B (PTP1B) and α-glucosidase. Subsequent isolation and characterization of the constituents by the use of HPLC-HRMS and NMR spectroscopy led to the identification of seven previously undescribed serrulatane diterpenoids together with nine known compounds, out of which three compounds showed potential antidiabetic activities. The work with solid-phase extraction (SPE) fractions of the crude leaf extract of *E. galeata* showed that one fraction (40% acetonitrile) exhibited potential synergistic effects with the chemotherapeutic drug SN-38 on SN-38 resistant HT29 cancer cells, and another fraction (60% acetonitrile) showed cytotoxic effects against three colon cancer cell lines (HT29, HCT116 and LoVo). The subsequent work led to the isolation and structure elucidation of a flavonoid (5,3',5'-trihydroxy-3,6,7,4'-tetramethoxyflavone) with SN-38-synergistic effects (efflux-pump inhibition) and six previously undescribed myoporone-derived analogs, out of which one showed cytotoxic effects (IC_{50} values of 29.48±1.85 µg/ml, 19.54±3.76 µg/ml and 29.87±2.84 µg/ml).

Not only in drug discovery has nature played an immense role, but also in the modern use of natural products as herbal drugs and supplements. The use of herbal drugs and supplements has emerged as a popular remedy for patients suffering from multiple sclerosis, since there is no curative treatment of this disease, and available treatments are only partially effective. The use of herbal

drugs and supplements concomitantly with prescribed medicine does however raise a possibility of herb-drug interactions, which is why it is important to address any safety issues associated with concomitant use. The third project in this thesis thus aimed at conducting a systematic literature review to investigate the potential interactions between selected conventional drugs and herbal drugs/supplements frequently used by MS patients. The results showed that very limited studies regarding herb-drug interactions with disease-modifying treatments were available, suggesting a need for more research within this topic. It was furthermore found that the daily recommended dose of products such as *Ginkgo biloba* and Ginseng should not be exceeded, and that non-standardized *Ginkgo biloba* preparations should preferably be avoided. No significant evidence for interactions between ginger, cranberry, vitamin D, fatty acids, turmeric, probiotics or glucosamine and the selected symptom-alleviating MS drugs were found, whereas there might be risks associated with chronic cannabis use and anti-depressive serotonin reuptake inhibitors. More studies are however needed to fully conclude on this.