

#### Medicinal Chemistry: Fundamental Principles for Small Molecule Optimization in Drug Discovery

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# Anti-cancer, anti-inflammatory and anti-oxidant activity of fractions and compounds isolated from endemic plant species of Sri Lanka

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Plant species have been commonly used as alternative or complementary therapy for a number of chronic diseases such as cancer and inflammation especially in developing countries such as Sri Lanka since ancient times. The undisputable therapeutic effects of plants have made researchers around the globe to discover bioactive compounds present in them. Sri Lanka is home to around 3700 floral species and of these, 24% is endemic to the country. Less than 1% of these plants have been scientifically evaluated. As such we have shown the bioactivity of two Sri Lankan endemic plants namely Wrightia antidysenterica (WA) and Osbeckia octandra (OO).

Dried and finely powered leaves, stem, root, flowers and the whole plant were subjected to sequential extraction with hexane, dichloromethane and methanol. Number of bioassays were used to determine the anti-oxidant, anti-lipase, anti-amylase, anti-inflammatory, anti-cancer, anti-bacterial, anti-tyrosinase activity of plant extracts. Subsequently the most active extracts were subjected to fractionation and compound isolation.

The methanol stem extract of WA and methanol whole plant extract of OO demonstrated the highest anti-oxidant activity compared to butylated hydroxytoluene (+ve control). The IC50 values for WA were 0.27 mg/ml, 0.20 mg/ml and 0.05 mg/ml, IC50 values for OO were 0.009 mg/ml, 0.03 mg/ml and 0.04 mg/ml and IC50 values for butylated hydroxytoluene were 0.11 mg/ml, 0.3 mg/ml, 0.02 mg/ml for 2,2-Diphenyl-1-picrylhydrazyl (DPPH), Ferric reducing antioxidant power (FRAP) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) assays respectively. On the other hand the methanol stem extract (IC50 0.31 mg/ml) of WA and methanol whole plant extract (IC50 0.19 mg/ml) of OO showed excellent antiinflammatory activity compared to aspirin (+ve control) (IC50 0.59 mg/ml) by human red blood cell membrane stabilization assays. Further, the WA stem extract showed an IC50 value of 0.75 mg/ml, while the OO whole plant extract demonstrated an IC50 value of 0.52 mg/ml compared to tamoxifen (+ve control- 0.02 mg/ml) against the MCF-7 breast cancer cell line illustrating that the extracts had slight cytotoxic activity. Extracts showed trivial activity for anti-lipase and anti-bacterial activity while none of the extracts showed anti-amylase activity and anti-tyrosinase activity. The methanol stem extract of WA and the methanol whole plant extract of OO were subjected to fractionation and 27 fractions were derived where 14 were found to be active. Out these 14 active fractions; Fraction 4 of WA was very active with IC50 values of 0.19 mg/ml, 0.13 mg/ml and >1 mg/ml and Fraction 7 of OO was active with IC50 values of 0.31 mg/ml, 0.26 mg/ml, >1 mg/ml for anti-oxidant (DPPH), anti-inflammatory and anti-cancer assays respectively. Pure compounds are being isolated and structure elucidation is being conducted. Currently compounds such as gallic acid, and quercetin have been found in OO. These results may provide an indication that, if these two plants are fully explored, they might have the potential of providing pharmaceutical agents for various chronic diseases such as inflammation. Thus more research is being conducted with these two endemic plants.