Isolation of modulators of Organic Anion Transporting Polypeptides (OATPs) from *Rollinia emarginata* Schlecht (Annonaceae)

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Organic Anion Transporting Polypeptides (OATPs) comprise a superfamily of sodium-independent membrane transporters which are involved in transporting numerous endogenous and exogenous substances. OATPs are expressed in different tissues such as intestine, liver, kidney and brain, and are responsible for the uptake of important drugs including cholesterol-lowering agents (statins), endothelin receptor antagonists (sartans), the anticancer drugs methotrexate, SN-38, paclitaxel and docetaxel, as well as the antibiotic rifampicin. Through a strategic collaboration, we search for novel small molecules from the organic extract of *Rollinia emarginata* Schlecht. (Annonaceae) that interact with the liver specific OATP1B1 and OATP1B3 applying a bioassay guided isolation approach. The organic extract was fractionated using different chromatographic techniques, and each fraction was tested for its effect on OATP1B1- and OATP1B3-mediated transport of 1µM estrone-3-sulfate and 0.1µM estradiol-17□-glucuronide. Several inhibitors, including both substrate-specific and non-specific, were isolated and chemically identified. For instance, the compound Quercetin 3-*O*-□-L-arabinopyranosyl (1 →2)□-L-rhamnopyranoside was shown to inhibit both OATP1B1- and OATP1B3-mediated transport of estradiol-17□-glucuronide by more than 90%, relative to control (DMSO). However, with respect to transport of 1µM estrone-3-sulfate it inhibits OATP1B1 by only 45% while, interestingly, stimulating transport mediated by OATP1B3 (2 fold over control). Thanks to our collaborative efforts, we were able to show that plants can be suitable source of small molecules that modulate OATPs using bioassay guided isolation approach.