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Studies on the human and rat OATP2B1 with coproporphyrin III

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Author Müller, Vanessa
Author at UniBasel Meyer zu Schwabedissen, Henriette ;
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Objective: Coproporphyrin III (CPIII) is a product of the heme biosynthesis and represents a potential biomarker for drug-drug interactions involving drug transporters. CPIII was shown to interact with the Organic Anion Transporting Polypeptide (OATP) 2B1. One aim of this study was to investigate whether hyperforin, known to interact with human OATP2B1, also interacts with the rat Oatp2b1-mediated transport of CPIII. We further tested the influence of two St. John's wort formulations with a high and a low hyperforin content, respectively. Since it is known that CPIII interacts with efflux transporters, a further aim was to investigate the influence of uptake and efflux transporters on the intracellular CPIII accumulation.
Methods: Transiently transfected HeLa cells overexpressing rOatp2b1 or hOATP2B1 were used to test the influence of hyperforin, Hyperiplant^{TM}and Rebalance^{TM}on the CPIII accumulation. To investigate the influence of the uptake and efflux transporters double transfection was performed with OATP2B1/ MRP2 and OATP2B1/ MRP3 and intracellular CPIII accumulation was determined. Successful transfection was proved using Western blot analysis.
Results: Hyperforin and Hyperiplant^{TM}showed an inhibition of the rOatp2b1-mediated CPIII transport, whereas Rebalance^{TM}, the St. John's wort formulation with a low hyperforin content, did not inhibit rOatp2b1. Furthermore, we were able to show an interaction of CPIII with MRP3, but not with MRP2.
Conclusion: We could show that besides human OATP2B1 also rat Oatp2b1 interacts with hyperforin. With the formulations we could further demonstrate that this interaction depends on the hyperforin content. By using double transfected HeLa cells, we found an interaction between OATP2B1/ MRP3, but not between OATP2B1/ MRP2.

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