ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology & Toxicology

Student: Daniela Uramová

Supervisor: Assoc. Prof. Přemysl Mladěnka, Pharm.D., Ph.D.

Title of diploma thesis: Pharmacokinetics of flavanones

The aim of the work was to summarize the available information regarding the fate of the flavanones in the human organism. These flavonoids are a common part of human diet, and therefore oral administration is the most relevant and examined. There are many obstacles in the digestive tract which are lowering their absorption. Flavanones in human food occur mainly in the form of glycosides, and therefore must be deglycosylated by the β glucosidase enzyme family. Aglycones are absorbed mainly in the small intestine. Flavonoids in the form of non-cleavable glycosides (e.g., rutinosides) are absorbed in the distal parts of the digestive system, after cleavage of the sugar component by intestinal bacteria. They also decompose the flavanone ring. This leads to substances with a phenylpropionic structure which can be absorbed. In general, flavanones are subject to extensive metabolism by cytochrome P450, not only in the liver but also in the enterocytes, which greatly limits their bioavailability. They are also rapidly conjugated with glucuronic or sulfuric acid. The resulting metabolites are predominantly secreted by the kidneys into the urine, but minor excretion may also occur in the stool. As a result of these prosesses, flavanones have low bioavailability.

Finally, we focused at interactions between flavanones and some co-administered drugs. Interactions can occur at several levels: cytochrome P450; or influx and efflux transporters. Interactions can either lead to increased bioavailability of co-administered drugs and to occurrence of unexpected side effects or, on the contrary, to reduce bioavailability and treatment failure.