# Metabolic Pharmacokinetics of *Rheum palmatum* and Emodin and Their Effects on Cyclosporine Pharmacokinetics

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## Abstract

Rhubarb is the dry root and root stock of *Rheum palmatum* L. (Polygonaceae). Anthraquinones including aloe-emodin, rhein, emodin and chrysophanol are the active constituents of rhubarb.

This study used HPLC gradient elution to simultaneously determine aloe-emodin, rhein, emodin and chrysophanol and their glycosides in decoctions of rhubarb prior to and after wine processing. The results indicated that rhein is the heighiest content of four anthraquinones, followed by emodin, aloe-emodin and chrysophanol in rhubarb. Only rhein occurs mostly as free form, others occurs mostly as glycosides. Both total and free anthraquinones were decreased after wine processing, whereas rhein glycosides increased and chrysophanol

glycosides remained substantially unchanged.

Furthermore, rats were administered with various decoctions equivalent to 5 g/kg after overnight fast. Blood was withdrawn via cardiopuncture and assayed by HPLC method prior to and after emzymatic hydrolysis with sulfatase and ß-glucuronidase, respectively. A simple, sensitive, and accurate HPLC method was developed for the determination of these anthraquinones and their conjugated metabolites simultaneously. The results showed that only rhein existed in part as free form (14 %), all anthraquinones were found predominantly as sulfates (44~58 %) and glucuronides (37~56 %) in bloodstream.

Cyclosporine is a commonly used immunosuppressive agent with narrow therapeutic range. Any factor influencing its blood level might threaten life. In this study, the rats were given cyclosporine alone and with emodin, decoctions of Da Huang or Hu Zhang, respectively. The blood cyclosporine concentration was determined by fluorescence polarization immunoassay. The results showed that the mean AUC of cyclosporine were decreased by 69.5 %, 65.0 % and 75.3 % after oral coadministration of cyclosporine with emodin, Da Huang and Hu Zhang, respectively. However, when coadministration of cyclosporine (i.v.) with Da Huang decoction (p.o); the AUC was increased by 102.8 % and the Clearance was decreased by 40.6 %. Therefore, it could be presumed that the lowering effect of Da Huang decoction in bioavailability occurred mainly at absorption site, and that was much more marked than the lowering in Clearance. We suggested that for the sake of efficacy and safety, the coadministration of Da Huang, Hu Zhang or herbs containing emodin with cyclosporine should be avoided.