Presystemic Metabolism of Glycosides in Herbs

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ABSTRACT

Glycoside is an important class of constituents in decoctions of Traditional Chinese Medicine (TCM). This study investigated the presystemic metabolism of the glycosides of flavones, anthraquinones, monoterpenes and triterpene in various animal feces.

Flavonoids are primarily present as glycosides in fruits, vegetables, beverages and Chinese herbs. It has been generally accepted that flavonoid glycosides reach the large intestine, where they are hydrolyzed to absorbable aglycones and further degraded by the intestinal microflora. The hydrolysis and degradation of hesperidin, naringin, rutin and phellamurin showed similar pattern when they were incubated with rabbit, rat and human feces. The isoflavonoid glycosides, genistin and daidzin, can be transformed into aglycone with rat and rabbit feces, however, puerarin cannot be hydrolyzed to daidzein with various feces. The result indicated that the C-glycoside cannot be hydrolyzed by intestinal bacteria. Among thirteen flavonoid aglycones, wogonin and diosmetin were among the less degraded ones for all three feces tested, indicating that the presence of a methoxy group on the A or B ring of the flavonoid seemed to protect the structure from bacterial degradation.

Catalpol is a monoterpene glucoside in Rehmanniae Radix. Catalpol is very unstable in artificial gastric juice. When catalpol were orally given to rats and mice, no parent form or metabolites can be detected in the serum.

Paeoniflorin is a monoterpene glucoside in Paeoniae Radix. The metabolism of paeoniflorin by various feces indicated that paeoniflorin was hydrolyzed to paeoniflorgenin (PG) by rabbit, rat, pig and human feces. When rats were orally administered with Paeoniae Radix decoction,

paeoniflorin was not present in serum and PG was found as a major metabolite. Noncompartment model was used for the calculation of pharmacokinetic parameters of paeoniflorgenin. The C_{max}, t_{max}, $t_{1/2}$, and AUC_{0-t} of PG were 8.0 μg/ml, 10 min, 126 min and 487.0 μg • min/ml, respectively.

Quercetin glucosides and rutin are bioactive glycosides present in onion and Huaimi, respectively. The sugar moieties of glycosides are different in two sources. The total quercetin contents were assayed by HPLC method after acid hydrolysis. Rat and human feces were used to investigate the difference between the microfloral metabolism of onion and Huaimi containing equal molar quercetin glycosides. The results indicated those in onion were much easier to be hydrolyzed to quercetin than Huaimi by both feces.

To investigate the presence of sulfatase in different species of animals, quercetin sulfates was incubated at 37℃ with artificial intestinal juice, β-glucuronidase, rat and human feces, respectively. We found that quercetin was significantly generated after incubation with rat and human feces. Therefore, sulfatase is present in rat and human gastrointestinal tract.

Aloe-emodin, rhein, emodin, chrysophanol and their glycosides are bioactive anthraquinone constituents of *Rheum palmatum.* The metabolism of rubarb decoction was investigated in rat feces suspension using HPLC. The result showed that the four anthraquinones constituents were profoundly increased during incubation, indicating that anthraquinone glycosides existed predominantly in rubarb.

Baicalin, baicalein, wogonin glycoside and wogonin are bioactive flavone constituents of *Scutellaria baicalensis*. The metabolism of Scutellariae Radix was investigated in rat feces suspension using HPLC. The hydrolysis and degradation of flavones in decoction of Scutellariae Radix (S), Scutellariae Radix fried with wine (SFW) and honey-treated Scutellariae Radix (HTS) showed similar pattern when they were incubated with rat feces.

Pure glycyrrhizin was hydrolyzed to glycyrrhetic acid in a greater extent than glycyrrhizin in licorice decoction by rat, pig and human feces, whereas rabbit feces oxidized glycyrrhetic acid to 3-dehydroglycyrrhetic acid and

resulted in less glycyrrhetic acid. This could explain the fact that oral dosing of pure glycyrrhizin resulted in much lower glycyrrhetic acid serum levels than that of licorice decoction in rabbits. The results indicated that rat and pig are proper animal models for the studies of the metabolism of pure glycyrrhizin and licorice decoction, whereas rabbit model is good for licorice decoction but not for pure glycyrrhizin.

In conclusion, it can be therefore presumed that glycosides are hydrolyzed to absorbable aglycones after oral dosing Chinese medicine decoctions. The lipophilic aglycones can be absorbable by enterocyte, whereas those of poor lipophilicity may be degraded by enteral microflora. Due to the similar pattern of metabolism shown for all tested animal feces except rabbits, it can be concluded that rats and pigs are better animal models for investigating the metabolism of herbal glycosides in human.