Ⅱ-101

랫트에서 신규 이소플라보놀 글리코사이드인 Talosin A의 약물동태학적 연구

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Pharmacokinetic Study of New Isoflavonol Glycoside, Talosin A, in Rats

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Objectives

The ovjectives of the present study was to evaluate pharmacokinetic profiles of newly isolated isoflavonol glycoside, talosin A and to compare with that of genistin. Moreover, A highly sensitive and specific atmospheric pressure electrospray ionization liquid chromatography - mass spectrometry method was developed for pharmacokinetic studies of genistin and talosin A in rats

Materials and Methods

Chromatography was carried out on a reversed-phase Zorbax Extended C18 column (3.5 μm, 4.6 mm×50 mm) and the mobile phase consisted of 35% 10 mM ammonium acetate (pH 4.0) and 65% acetonitrile with a flow rate of 0.4 mL/min. Inter-assay CV values were less than 13.36% and the nominal concentrations ranged from 93.09 to 116.25%. Intra-assay CV values were less than 12.05% and the nominal concentrations ranged from 96.35 to 118.35%. The validated method was successfully applied to the characterization of the pharmacokinetics of genistin and talosin A in rat plasma after their oral administration at the dose of 20 mg/kg of BW, respectively.

Results

After oral administration of genistin, the peak plasma (C_{max}) of 2.41±0.51 μg/mL as a genistein was reached at 4.00±2.00 h (T_{max}) and the elimination half-life ($t_{1/2\lambda Z}$) was 2.36±1.01 h. After oral administration of talosin A, the C_{max} of 3.09±1.59 μg/mL as conjugates talosin A was reached at 1.13±0.63 h. The $t_{1/2\lambda Z}$ was 5.33±1.53 h. Talosin A was converted into genistein as well as conjugates of genistein and talosin A in rat plasma. We elucidated talosin A metabolism in the gastrointestinal tract of rats much differed as compared with genistin.

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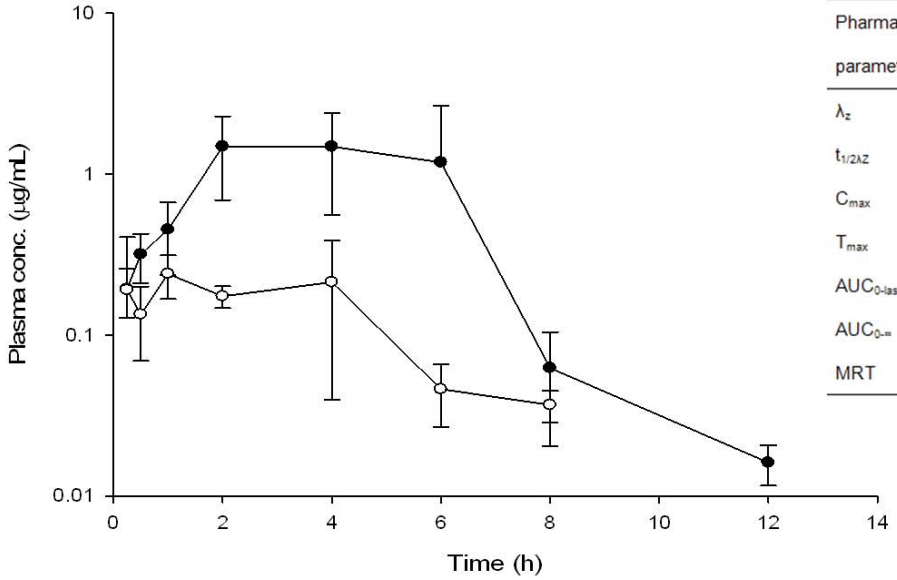
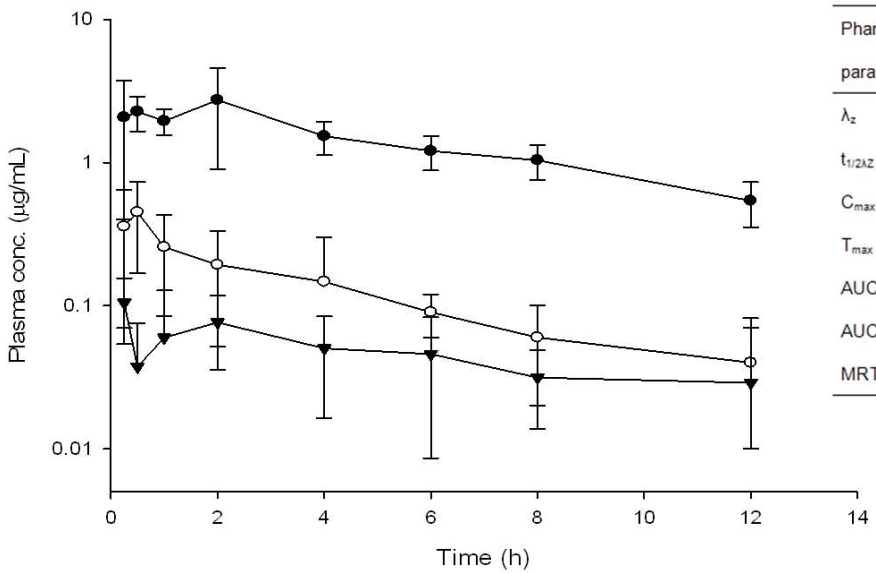


Pharmacokinetic parameters*	Units	Mean±SD
λ_z	1/hr	0.34±0.18
$t_{1/2\lambda Z}$	hr	2.36±1.01
C_{max}	μg/mL	2.41±0.51
T_{max}	hr	4.00±2.00
AUC_{0-last}	hr*μg/mL	11.42±3.04
$AUC_{0-\infty}$	hr*μg/mL	11.54±2.91
MRT	hr	3.95±0.28

Figure 1. Mean plasma concentration-time curve of genistein after oral administration of genistin at 20 mg/kg in rats (n=4). Filled circle (●), total plasma genistein; empty circle (○), free plasma genistein. Free genistin was not detected in rat plasma samples after oral administration of genistin.



Pharmacokinetic parameters*	Units	Mean±SD
λ_z	1/hr	0.14±0.04
$t_{1/2\lambda Z}$	hr	5.33±1.53
C_{max}	μg/mL	3.09±1.59
T_{max}	hr	1.13±0.63
AUC_{0-last}	hr*μg/mL	16.62±4.70
$AUC_{0-\infty}$	hr*μg/mL	21.10±7.17
MRT	hr	7.65±1.33

Figure 2. Mean plasma concentration-time curves of talosin A and genistein after oral administration of talosin A at 20 mg/kg in rats (n=4). Filled circle (●), total plasma talosin A; empty circle (○), total plasma genistein; filled triangle (▼), free plasma genistein. Free talosin A was not detected in rat plasma samples after oral administration of talosin A.

Conclusion

There was much difference in the oral absorption and metabolism between talosin A and genistin. Further study is needed for its potential toxicity and metabolic characteristics. The validated method was successfully applied to the characterization of the pharmacokinetics of genistin and talosin A in rat plasma after oral administration.