Pharmacokinetics of Arctigenin in Rats by Using Liquid Chromatography-Tandem Mass Spectrometry
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Purpose
Arctigenin is the main active ingredient of Fructus Arctii, which has been reported with a variety of therapeutic activities including anti-cancer, anti-inflammation, anti-virus, and anti-obesity effects. This study aimed to develop a simple and sensitive liquid chromatography-tandem mass spectrometry (LC/MS/MS) method for the determination of arctigenin in biological samples and evaluate pharmacokinetics of arctigenin in rats.

Methods
Arctigenin was administered to male Sprague-Dawley (SD) rats by intravenous injection at 3 mg/kg (n=4) or by oral administration at 50 mg/kg (n=4) and plasma samples were collected. To determine the renal and fecal excretion of arctigenin, arctigenin was given by oral administration (n=5) and urine and feces samples were collected for 48 h. Arctigenin concentrations in the biological samples were analyzed by a newly developed LC/MS/MS assay. The assay utilized a single step protein precipitation with methanol and the mobile phase consisted of 100% methanol and water containing 0.1% formic acid (65:35 v/v). Arctigenin and the internal standard (psoralen) were monitored using a positive electrospray turbo ionspray mode with multiple reaction monitoring transitions of m/z 373.2 → 136.9 and m/z 187.2 → 130.9, respectively. The pharmacokinetic parameters of arctigenin were analyzed by noncompartmental analysis.

Results
The lower limit of quantification (LLOQ) of arctigenin was 5 ng/mL in the plasma, 15 ng/mL in the urine, and 40 ng/mL in the feces. The intra- and inter-day accuracy of arctigenin at LLOQ and matrix-matched quality control samples ranged 97.4 – 105.7% and 97.2 – 105.9%, respectively. The intra-day precision was within 4.80% and the inter-day precision was within 5.92%. Following intravenous injection, arctigenin plasma concentration was rapidly declined with the terminal half-life (t₁/₂) of 0.27 ± 0.02 h. Upon oral administration, it was rapidly absorbed (Tₘ₉₉ < 5 min) with a bioavailability of 0.12%. Renal clearance of arctigenin was 103.1 ± 78.2 mL/h and 8.59% of the dose was recovered from the feces after oral administration.

Conclusion
A simple, rapid, and sensitive LC/MS/MS assay for quantification of arctigenin in the rat plasma, urine, and feces was developed and validated. Arctigenin exhibited a relatively short elimination half-life in rats. Following oral administration, arctigenin was rapidly absorbed and showed low oral bioavailability. The LC/MS/MS assay and pharmacokinetics of arctigenin in rats in the present study may provide useful tool for further preclinical studies as well as clinical studies of arctigenin.