Thesis Title : Absorption, metabolism and excretion of 2,4,3′,5′-Tetrahydroxystilbene in volunteers after oral administration of purified extract of Puag-haad.

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ABSTRACT

Purification of Puag-haad by extraction with diethyl ether and recrystalization in water yielded a compound proved to be 2,4,3′,5′-tetrahydroxystilbene dihydrate.

A High Performance Liquid Chromatographic method measuring concentrations of 2,4,3′,5′-tetrahydroxystilbene in urine and plasma were developed. The method employs a one-step extraction procedure by using diethyl ether as a solvent followed by analysis on a reversed-phase high performance liquid chromatography on μ-bondapak C_{18}(10 μm) with UV detection at 313 nm and 48% methanol in water(v/v) as a mobile phase. Phenacetin was used as an internal standard for quantitation. The detection limit for 2,4,3′,5′-tetrahydroxystilbene in urine and plasma were 1.0 mcg/ml

(20 ng of the amount). In urine assay the mean recoveries were 92.3 % with 3.17 % coefficient of variation and in plasma assay were 90.7 % with coefficient of variation of 2.52 %.

The method had been applied to the analysis of 2,4,3',5'-tetrahydroxystilbene in urine and plasma following an oral dose of 3000 mg of purified Puag-haad to nine healthy male volunteers. This method was rapid, specific and accurate and would be suitable for pharmacokinetic studies.

2,4,3',5'-tetrahydroxystilbene kinetics were studied in nine healthy male volunteers, their mean age 33.2 ± 5.2 years. Plasma levels and the cumulative of 2,4,3,5-tetrahydroxystilbene excreted in urine were determined by HPLC. Levels rose after drug administration reaching a maximum concentration of 0.702 ± 0.347 mcg/ml in 1.38 ± 0.16 hr. The apparent absorption rate constant was 0.74 ± 0.09 hr^{-1}. The mean area under the plasma concentration time curve was 2.5530 ± 1.1439 hr.mcg/ml. The mean elimination half life was 0.96 ± 0.11 hr corresponding to an elimination rate constant of 0.73 ± 0.08 hr^{-1}. The mean renal clearance was 13.19 ± 2.95 ml/hr/Kg. The detection of possible metabolite in urine by TLC method found only 2,4,3',5'-tetrahydroxystilbene. 2,4,3',5'-tetramethoxystilbene and 2,4,3',5'-tetraacetoxystilbene were not detected. No side effect was reported by seven volunteers and only mild nausea was reported by two volunteers.