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Identification of urinary metabolite(s) of CKD-712 by gas chromatography/mass spectrometry in rats

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Examination was made of the urinary metabolite(s) of CKD-712, which is a chiral compound, named S-YS49 derived from higenamine (one component of *Aconite spp.*) derivatives. First of all, to analyze the metabolite(s) of CKD-712, a simple and sensitive detection method for CKD-712 was developed by using gas chromatography-mass spectrometry GC/MS). Urine was collected from adult male Sprague-Dawley rats 250±10g) in metabolic cage for 24hr after oral administration of 100 mg/kg of CKD-712. The recovery of CKD-712 after extraction and concentration with AD-2 resin column was above 90 % from rat urine. The detection limits of CKD-712 in urine was approximately 0.1 ng/mL. It has well been suggested that isoquinoline possessing catechol moiety such as CKD-712 should be subjected to the catechol-O-methyl transferase activity in vivo. We detected three major peaks of presumed CKD-712 metabolites in the total ion chromatogram obtained from the rat urine sample after oral administration of CKD-712. From these results, it is assumed that the urinary metabolites are mono-methylation in the naphthyl moiety (metabolite I), methylation at the C-6 or 7 hydroxy group in the isoquinoline moiety and hydroxylation at in the naphthyl moiety (metabolite II), and methylation at the C-6 or 7 hydroxy group in the isoquinoline moiety (metaboliteIII).