

## 9 $\alpha$ -フルオロメドロキシプロゲステロンアセテートのラット体内薬物動態

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### Pharmacokinetics of 9 $\alpha$ -Fluoromedroxyprogesterone Acetate in Rats: Comparison with Medroxyprogesterone Actetae

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**ABSTRACT** Medroxyprogesterone acetate (MPA) is widely used in endocrine therapy for breast cancer and other diseases. Recently, it has been demonstrated that 9 $\alpha$ -fluoromedroxyprogesterone acetate (FMPA) also has anti-tumor activity in chemical-induced rat mammary tumor and its activity is greater than that of MPA. In the present study, the physico-chemical properties of FMPA and MPA and their pharmacokinetics in female rats were investigated. Partition coefficient (log P) of FMPA and MPA were 3.1 and 3.8, respectively, while the solubilities of FMPA and MPA in phosphate buffer saline were 3.8 and 1.1 mg/mL, respectively. When the two agents were intravenously or orally administered into female rats, there was no significant difference between their plasma concentrations. However, unmetabolized drug excreted into urine accounted for 4.7 and 0.7% of the intravenous dose of FMPA and MPA. Assuming the well-stirred model, hepatic intrinsic clearances of FMPA and MPA were estimated to be 64 and 293 L/h per kg, respectively. In addition, the free fraction of FMPA in blood is estimated to be higher than that of MPA, which may explain the higher anti-tumor activity.

抄録 9 $\alpha$ -フルオロメドロキシprogesteronアセテート (FMPA)のラット体内薬物動態をメドロキシprogesteronアセテート (MPA)との比較において行った。

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