新生ラットへの経口投与技術を用いた化学物質の影響評価

Evaluation for impacts of chemical substances using an oral administration technique to neonatal rat

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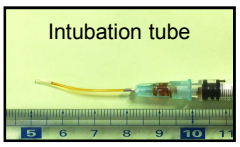
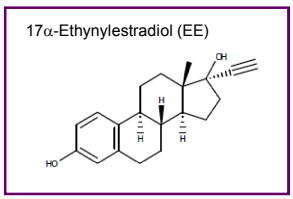
Effects of chemicals taking via foods by infants have been concerned. We have evaluated effects of neonatal exposure of 17α-ethynylestradiol (EE), a model compound for endocrine disrupting chemicals, by administering for 5 days from postnatal day one using the oral administration technique with an intubation tube. As illustrated in Fig. 2, the treated animals were monitored physical development, such as body weight, eyelid opening, vaginal opening, and estrous cycle, and were terminated on postnatal week 22-23 for necropsy.

Table 1 Serum concentration of EE after oral treatment of 2 ng/g BW of EE (mean ± SEM) [1)]

Time after treatment	Samples	EE (pg/mL)
24 hrs after the 1st treatment	4	12.8 ± 3.4[a]
6 hrs after the 5th treatment	3	47.3 ± 8.1[b]
24 hrs after after the 5th treatment	3	6.7 ± 2.1[a]

Different characters shown in the serum EE concentration represent significantly difference.





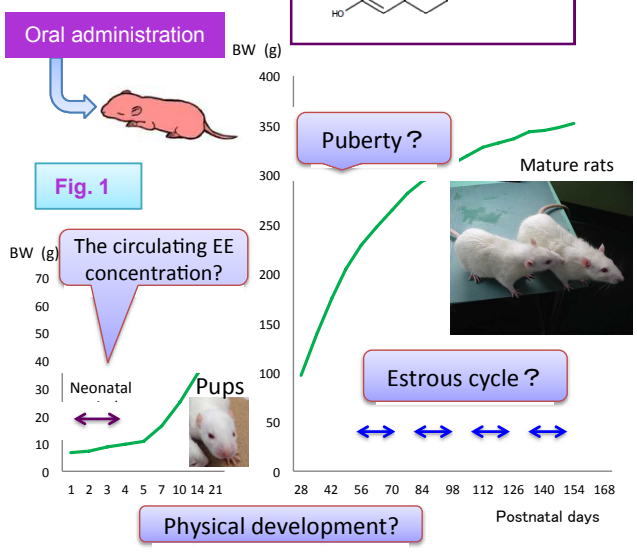
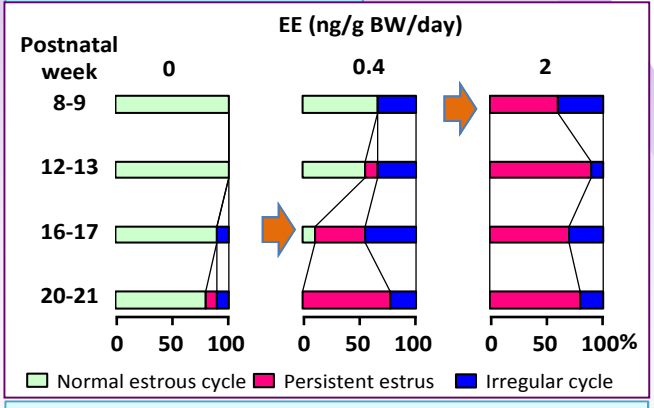


Fig. 2 Effects on estrous cycle[1)]



Orally administered EE was confirmed to enter into the circulation (Table 1), and the treatment did not affects the physical development. However, the treatment accelerated the onset of delayed effects, including arrest estrous cycle (Fig. 2), formation of cystic follicles without luteal formation in the ovary (Fig. 3), and mammary gland hyperplasia (Fig. 4), dose-dependently. The present study using an oral administration technique to neonatal rats clearly showed a slight increase in the circulating estrogens during the neonatal period exerts irreversible delayed effects[1)].

Fig. 3 Cystic follicle formation and lack of corpus luteum at the terminal necropsy[1)]

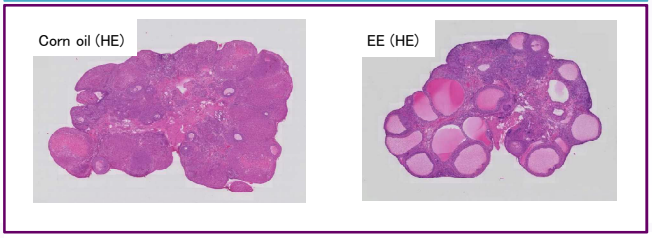
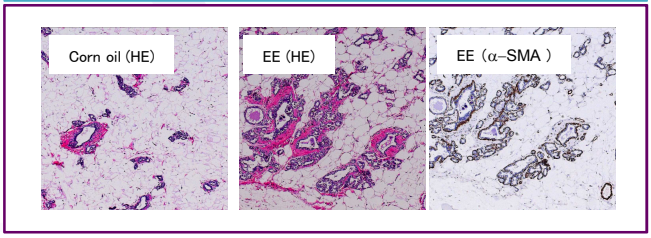


Fig. 4 Mammary gland Hyperplasia (Postnatal week 22-23) at the terminal necropsy[1)]



The oral administration technique applied in the present study has been published by Watanabe et al. in 2003[2)], and they found no adverse effects on the animals. The technique may apply to wide field including the area where efficacies of chemical substances on mental, physical or intellectual development are evaluated, since there is accumulated basic knowledge and established evaluating methods in broad range of fields using rats.

References
1)Shirota, M., et al., J. Toxicol. Sci. 40, 727-738 (2015)
2)Watanabe, C., et al., Congenit. Anom (Kyoto) 43, 177-179 (2003)
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