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Ampiroxicamの毒性試験

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Acute, Subacute and Chronic Toxicity Studies of Ampiroxicam in Rats

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The acute, subacute and chronic toxicities of ampiroxicam, a newly developed nonsteroidal anti-inflammatory agent and a pro-drug of piroxicam, were evaluated in Sprague-Dawley rats.

The acute oral LD_{50} values of ampiroxicam were 1798 mg/kg in male rats and 747 mg/kg in female rats.

In the subacute toxicity study, male and female rats were treated orally with ampiroxicam (14, 7, 3.5 and 1.4 mg/kg) for 3 months. Vehicle group was used as a control. No deaths occurred at any dose level. Growth inhibition was noted in both sexes at 14 mg/kg. Slight decreases of hemoglobin, hematocrit and RBC were observed in both sexes at 14, 7 and 3.5 mg/kg. Slight decreases of total protein, albumin and globulin were seen in males at 14 mg/kg and in females at 14 and 7 mg/kg. Granulomatous whitish nodules in the wall of the small intestine were noted in females at 14 and 7 mg/kg. There were erosions in the glandular stomach in both sexes at 14 and 7 mg/kg and in males at 3.5 mg/kg. Extramedullary hematopoiesis in the spleen, granulocytic and/or erythrocytic hyperplasia in the bone marrow, and mesenteric lymphadenitis were found in females at 14 and 7 mg/kg. Most changes are considered to be complications related to the ulcerative lesions of the gastrointestinal tract. The no-effect dose level is estimated to be 1.4 mg/kg/day. In a 8-week recovery study, most parameters examined were found to be comparable with those of controls.

In the chronic toxicity study, male and female rats were treated orally with ampiroxicam (3.5, 1.4 and 0.7 mg/kg) for one year. Vehicle group was used as a control. No drug-related deaths occurred at any dose level. A slight growth inhibition was observed in females at 3.5 mg/kg. Hematological, blood chemical and histopathological changes similar to the results in the subacute toxicity study were noted in females at 3.5 mg/kg. In addition, renal papillary necrosis was found in females at 3.5 mg/kg. The no-effect dose level is considered to be 1.4 mg/kg/day.

Key words: Ampiroxicam／Acute／Subacute／Chronic toxicity (rat).

緒　言

ampiroxicamはファイザー社で，piroxicamのpro-drugとして開発された経口非steroid性酸性抗炎症薬である．その化学名は，(±)-4-[1-(ethoxycarbonyloxy) ethoxy]-2-methyl-*N*-2-pyridyl-2*H*-1, 2-benzothiazine-3-carboxamide 1, 1-dioxideである．

今回，著者らは，ラットを用いてampiroxicamの経口急性毒性，経口3カ月および1年毒性試験を実施したので，その成績を報告する．

実験材料および実験方法

1. 被験物質

ampiroxicamは，Fig 1に示した化学構造を有する白色～帯黄白色の結晶性の粉末で，水にほとんど溶けない．

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