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Amlodipineの急性，亜急性および慢性毒性試験

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Acute, Subacute and Chronic Toxicity Studies of Amlodipine in Rats

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Acute, subacute and chronic toxicities of amlodipine, a calcium channel blocker, were evaluated in Sprague-Dawley rats. The acute oral LD_{50} values of amlodipine were 393 mg/kg in males and 686 mg/kg in females. In the subacute oral toxicity study, in which amlodipine was administered at 30, 10 and 3 mg/kg for 3 months, all rats tolerated the drug well. No drug-related deaths occurred at any dose level. At the top dose of 30 mg/kg, salivation and growth inhibition were observed. Increases in urinary volume accompanied by increased excretion of electrolytes and decreases in serum electrolytes were noted. Slightly increased BUN and relatively increased heart weight were observed. The main histopathological finding was mild thickening of the zona glomerulosa of the adrenals. There were alterations in urinary excretion of electrolytes at 10 mg/kg. The no-effect dose level of amlodipine is considered to be 3 mg/kg/day. The rats were examined after one-month withdrawal of the drug following the three-month dosing. In the chronic toxicity study, the rats were treated orally with amlodipine (25, 10, 2 mg/kg) for one year. Some deaths occurred at the top dose level. Mild growth inhibition was observed in males receiving 25 or 10 mg/kg and in females receiving 25 mg/kg. Other results were comparable to those in the subacute toxicity study. The no-effect dose level in the chronic toxicity study with amlodipine is considered to be 2 mg/kg/day.

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

緒　言

amlodipine besilate（以下amlodipineと略）は，Phizer社が開発したdihydropyridine系のCa拮抗薬で，持続性の降圧作用を有し(山中ら，1991)，臨床では1日1回の投与で有効である．その化学名は，(±)-3-ethyl 5-methyl 2-[(2-aminoethoxy) methyl]-4-(*o*-chlorophenyl)-1, 4-dihydro-6-methyl-3, 5-pyridinedicarboxylate benzenesulfonateである．

今回，著者らは，amlodipineのラットでの経口急性毒性，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

amlodipineはFIG 1に示す化学構造を有する白色

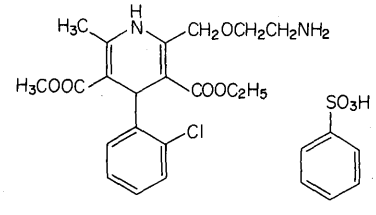

FIG 1　Structure formula of amlodipine.

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