Coronary Dilator Effect of MCI-176, a New Calcium Channel Blocker, in Dogs

DAIJIRO HORII and AKIRA ISHIBASHI

Tsukuba Pharmaceutical Laboratory, Research Center, Mitsubishi Chemical Industries Co. Ltd., 8-5-1 Chuou Ami-cho, Ibaraki 300-03


Effects of MCI-176, 2-(2, 5-dimethoxyphenylmethyl)-3-(2-dimethylaminoethyl)-6-isopropoxy-4 (3H)-quinazolinone hydrochloride, on coronary and aortic blood flows, mean blood pressure and heart rate were investigated in comparison with those of diltiazem in anesthetized dogs. MCI-176, like diltiazem, dose-dependently increased coronary and aortic blood flows and decreased mean blood pressure. In producing these effect MCI-176 was slightly but significantly more potent than diltiazem. Heart rate tended to increase with MCI-176, whereas it tended to decrease with diltiazem. ——— MCI-176 ; calcium channel blocker ; coronary blood flow ; dog

MCI-176, of which chemical structure is shown in Fig. 1, is a new potent calcium channel blocker selected from many quinazolinone derivatives (Sekiya et al. 1986*). The present article reports preliminarily its effects on coronary flow and cardiohemodynamics in anesthetized dogs. Mongrel dogs of either sex weighing 9-15 kg were anesthetized with pentobarbital sodium 35 mg/kg, i.v. Under artificial respiration the chest was opened at the fourth intercostal space. Blood flows through the left circumflex coronary artery and ascending aorta were measured with non-cannulating type probes. Mean blood pressure was measured with an electromanometer at the femoral artery. Heart rate was measured with a tachometer triggered by pulse pressures. In 12 dogs, both MCI-176 and diltiazem (30 and 100 μg/kg i.v., respectively) were administered into the same animals. The data

![Chemical structure of MCI-176](image)

Received May 9, 1986 ; accepted for publication July 12, 1986.

obtained were analyzed by the paired t-test. The basal coronary and aortic blood flows, mean blood pressure and heart rate were 37 ± 4 ml/min and 1.6 ± 0.5 liter/min, 104 ± 5 mm Hg, and 174 ± 7 beats/min, respectively. As shown in Fig. 2, MCI-176 increased coronary flow by 14.7 ml/min at 30 μg/kg and by 24.1 ml/min at 100 μg/kg. It increased aortic flow by 250 ml/min at 30 μg/kg and by 390 ml/min at 100 μg/kg and heart rate by 1.9 beats/min at 30 μg/kg and by 2.5 beats/min at 100 μg/kg. MCI-176 decreased mean blood pressure by 19 mm Hg at 30 μg/kg and 25 mm Hg at 100 μg/kg. Essentially similar results were obtained with diltiazem, although heart rate tended to decrease with diltiazem. In producing these effects, however, MCI-176 was slightly but significantly (p < 0.05) more potent than diltiazem. The difference in potency between MCI-176 and diltiazem is thought to derive from the difference in calcium antagonistic potencies judging from the results obtained in our laboratory (unpublished observations).

Fig. 2. Peak changes induced by MCI-176 (●–●) and diltiazem (○—○) in coronary flow (CF), aortic blood flow (AF), mean blood pressure (MBP) and heart rate (HR). Each value represents the mean ± s.e. of 12 dogs. * significant difference between values obtained with MCI-176 and those with diltiazem (p < 0.05).