Short communications

Effect of synthetic bradykinin on contractile tension of human saphenous vein strips

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The ability of synthetic bradykinin to contract isolated, helically-cut human saphenous vein strips was studied *in vitro*. Bradykinin (0·05–2·0 μg/ml) consistently failed to contract human vein strips. Similarly prepared rabbit aortic strips also failed to contract when exposed to bradykinin in the concentration range studied. Bradykinin-insensitive vein and aortic strips responded with substantial increases in contractile tension when exposed to prostaglandin E_2, noradrenaline, histamine and KCl. However, bradykinin (0·1 μg/ml) was capable of relaxing human vein strips, which had contracted in response to prostaglandin E_2.

Bradykinin produces a variable effect on contractile tension of various isolated vascular smooth muscle preparations (e.g., see Somlyo & Somlyo, 1970; Garrett & Brown, 1972; DePasquale & Burch, 1968; Winkelmann, Sams, Mitchell & Bohr, 1969; Gulati, Parikh & Umar, 1968; Starr & West, 1966; Ishioka, Matsumara, Honda, Sagara & Shimamoto, 1969; Hughes & Vane, 1967; Jaques, 1970). Of particular interest is the purported selective venoconstrictor effect of bradykinin (Hauck & Gillis, 1969).

During the course of preliminary experiments in which the effects of anti-inflammatory drugs on isolated human saphenous vein strips were studied (Levy, 1972), it was found that synthetic bradykinin (0·05–0·5 μg/ml) failed to constrict these tissues. At first it was thought that this might be due to the general non-reactivity of some veins resulting from experimental conditions under which the tissues were obtained. However, it has now been shown that synthetic bradykinin (Sandoz lot No. 69055) in a concentration range of 0·05–2·0 μg/ml consistently fails to constrict any spirally cut human saphenous vein strips which are reactive to other agonists.

Methods.—Helically-cut vein strips were prepared from fresh femoral saphenous vein segments obtained from patients undergoing aortocoronary bypass procedures, using methods described previously (Levy & Richards, 1964). Briefly, the vein segment obtained at surgery was transported to the pharmacology laboratory in oxygenated Krebs-Henseleit solution. Helically-cut strips (20 mm) were cut from the vein, and mounted in a myograph for recording contractile tension. Wet weight of these preparations ranged from 85–198 mg. An initial 2·0 g of resting tension was applied to the tissues. They were equilibrated for 90 min, then tension was readjusted to 2·0 g before starting the experiments. All experiments were done at 37·5° C. The synthetic bradykinin (BRS 640) used in these studies was provided by Sandoz Pharmaceuticals, Inc. Fresh ampoules of synthetic bradykinin were used for each experiment. The reactivity of the vein strips was confirmed by also challenging the tissues with prostaglandin E_2 (Upjohn), histamine (Lilly), noradrenaline (Winthrop) and KCl.

Results.—In all human femoral saphenous vein strips studied, bradykinin (0·05–2·0 μg/ml) failed to elicit a contraction. Vein strips that were completely refractory to bradykinin reacted with a substantial increase (0·3–3·0 g) in contractile tension to agents such as prostaglandin E_2 (5·68 μM), noradrenaline (0·6 μM), histamine base (9·0 μM) and KCl (60 mM). However, bradykinin (0·1 μg/ml) relaxed human saphenous veins which had contracted in response to prostaglandin E_2. Under the same experimental conditions, bradykinin (0·05–0·5 μg/ml) also failed to constrict isolated rabbit aortic strips.

Discussion.—The finding that bradykinin failed to constrict rabbit thoracic aortic strips agrees with those recently reported by Garrett & Brown (1972). They found that none of their rabbit aortic strips responded to synthetic bradykinin (Sigma Chemical) in the range of 0·05–0·5 μg/ml. They observed that only 42% of their preparations were sensitive to bradykinin, and then only in concentrations of 1, 3 or 9 μg/ml. DePasquale & Burch (1968) showed that 17 out of 22 canine venous (mesenteric and femoral) strips

constricted to bradykinin (0·125 μg/ml). Winkelmann *et al.* (1969) observed that bradykinin (1,250 μg/ml) caused contraction of all canine mesenteric and cutaneous arteriole strips (200–500 μm o.d.). Rabbit mesenteric and cutaneous vascular preparations failed to respond. However, rabbit pulmonary vessels do contract to bradykinin (1–10 μg/ml) (Starr & West, 1966). Isolated caval, jugular, saphenous and femoral veins of both rabbits and pigs constrict when exposed to bradykinin (0·1–0·5 μg/ml) (Jaques, 1970).

The negative findings with isolated human saphenous vein strips described here thus add to the list of vascular preparations which fail to constrict with bradykinin. I interpret this finding as representing a true species difference to bradykinin since rabbit saphenous veins do contract on exposure to the peptide (Jaques, 1970). The results do not exclude the possibility, however, that human vascular preparations from other segments of the circulation might constrict to bradykinin.

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