ip. The rat paw volume was measured along with time by the mercury method described by Van Arman *et al.* (1), and three constants were computed for each animal. Specification of A and B was conjectured on the basis of the results in the blueing experiment. The average values of 4 rats with standard deviations are given in the table which also includes the calculated values of peak time T_m and peak size Y_m .

It will be seen that the value of C is largely reduced and A increased by pretreatment with BOL 148, whereas the value of B is reduced. This fact indicates that the swelling force Ce^{-At} is affected by the antagonist in the direction of depressing the edema. Similar patterns of the change in three constants have been noted in other cases of inciter-antagonist combination. In other words, many anti-inflammatory agents are likely to exert seemingly potent effect in depressing the experimental edema only if given at an adequate time prior to the inciter injection. They are protective rather than curative in this sense. Further study is underway.

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PRESSOR MECHANISM OF VINCRISTINE SULFATE

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Studying the pharmacological activities of vincristine sulfate (VCR), one of the alkaloids isolated from *Vinca rosea* Linn. by Svoboda *et al.* (1), Anderson *et al.* (2) observed the pressor, positive chronotropic and respiratory stimulating effects in dogs. Since no action mechanisms of these pharmacological effects were reported, the authors attempted to clarify its pressor mechanisms.

Pressor effect of VCR (0.1–1.0 mg/kg, i.v.) was observed in dogs, cats, rabbits, guinea-pigs and rats under pentobarbital or urethane anesthesia. Fig. 1 shows the pressor effects of VCR in cats. The carotid blood pressure increased during first 60 minutes after the administration, and then gradually returned to normal. In cats, dogs, rabbits and guinea-pigs, VCR was characteristic of slow and long lasting pressor substance. On the contrary, pressor effect in rats was temporal lasting about 10 minutes.

Pressor effect of VCR was abolished in the vagotomized spinal cats (Fig. 1), and was slightly potentiated by the intra-carotid arterial administration. Pretreatment of an α -adrenergic blocker, dibenamine (2 mg/kg, i.v.), which reversed the pressor effect of epinephrine, markedly inhibited the pressor effect of VCR. The pressor effect of VCR was also completely abolished by the reserpine pretreated on the previous day (1.5 mg/kg, s.c.), while the pressor effect of tyramine was depressed to one half by the same treatment.

No effects were observed on the spontaneous movements of guinea-pig isolated atrium and rabbit isolated intestine by the administration of VCR into the organ bath (Magnus method). Increases of perfusate was

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FIG. 1. Effects of vincristine sulfate on the carotid blood pressure in cats.

recognized in the rabbit isolated ear artery (Kraukow-Pissemiski method) by the application of VCR in a dose of 1 mg, in which epinephrine (1 μ g) caused about 80% decreases of perfusate.

These data suggest that the pressor effect of VCR in cats and other animals might be caused by the following pathway: excitation of vasomotor center—via spinal cord—gradual release of norepinephrine from peripheral sympathetic nerve terminal—excitation of α -adrenergic receptor in the blood vessels—vasoconstriction—gradual increase of blood pressure.

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BIOLOGICALLY ACTIVE SYNTHETIC FRAGMENTS OF BRADYKININ

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Bradykinin, Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg, is released from bradykininogen by the action of kallikreins and brings about smooth muscle stimulation, vasodilation, increase in capillary permeability, accumulation and migration of leucocytes and pain production. It is well known that so-called kininase, for example catheptic carboxypeptidase B and carboxypeptidase N, destroy bradykinin by cleaving the peptide bond of the nonapeptide, producing pharmacologically inert peptides (1, 2). However, there is a possibility