A SIMPLE MODEL FOR RAT PAW EDEMA, TIME-COURSE STUDY

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A biometric analysis of the rat paw edema was described by Van Arman et al. (1), who fitted a quadratic curve to the time-course of the swelling volume.

We have attempted to describe the time-course of the swelling by a model in which the size of edema is regarded as the reflection of the dynamic balance between two forces, swelling and antiswelling (2). This simple model has some similarities to that for drug distribution kinetics (3), and shows fairly good fitness to some types of experimental edema. The hypotheses involved are: 1) the swelling force be an exponential function of time, \( \dot{y}_+ = Ce^{-At} \), and 2) the antiswelling force be linearly proportional to the increased volume existing, \( \dot{y}_- = -By \). The solution of the combined differential equation gives: \( Y = \frac{Ce^{At} - Ce^{At}}{A-B} \), where \( Y \) is the increased volume of the paw at time \( t \) following the inciter injection to the paw, and \( A, B \) and \( C \) are constants specific to a given experimental condition.

Eight curves with different \( A, B \) and \( C \) values are given in Fig. 1-A, \( \log_e Y \) being plotted against \( t \). In Fig. 1-B are plotted two curves, the constants of which have been computed from experimental data of rat paw edema induced by 5-hydroxytryptamine, 100 \( \mu \)g, with and without pretreatment of BOL 148, 2 mg/kg.

![Fig. 1](image_url)

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.

REFERENCES

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 Lian. 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 $\alpha$-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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