certain virus suspensions on host cells which have been heavily irradiated with ultraviolet light. Not requiring a co-factor, T2 virus rapidly lyses *E. coli* B irradiated with some 200 to 500 lethal doses of ultraviolet light. Such lysis proceeded in a summary manner, *i.e.*, without the multiplication of virus which accompanies lysis of normal host cells. In the case of T2 virus, this reaction is accomplished by a lytic substance which is separable from the major portion of the virus particles.[5]

T4 and T6 virus display no such activity in the absence of a suitable co-factor to enhance their rates of adsorption on the host cells; with a co-factor present, T4 and T6 each react in a manner related to the concentration and activity of the co-factor. The results of a comparison of the activities of *dl*-tryptophane and *dl*-Bz-2-methyltryptophane are given in Fig. 1. It is

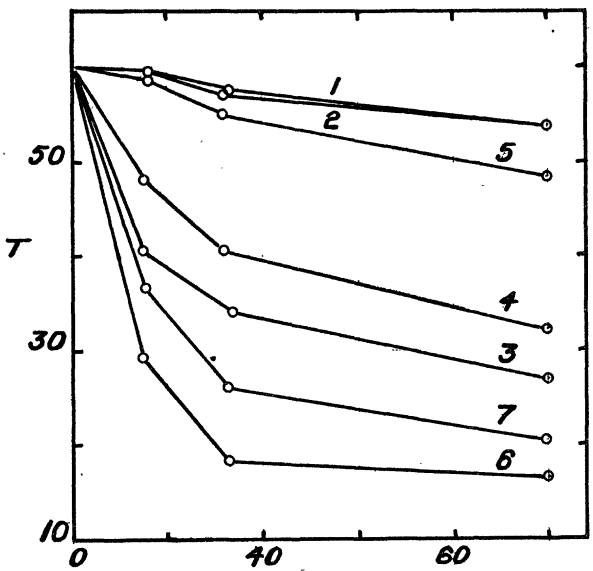


FIG. 1. The lysis of UV-irradiated *E. coli* strain B by viruses T4 and T6 in the presence of co-factors *dl*-tryptophane and *dl*-Bz-3-methyltryptophane. The bacteria in an actively multiplying state in ammonium lactate medium were irradiated in a quartz tube with about 500 lethal doses of ultraviolet light from a H-4 lamp with the outer glass shell removed. 5 cc of the irradiated bacterial suspension were then added to each of seven colorimeter tubes which contained in 0.4 cc of the ammonium lactate medium: 1. Control. 2. $0.95 \times 10^{10}$ T4 virus particles. 3. $0.95 \times 10^{10}$ T4 virus particles + 0.204 mg *dl*-tryptophane. 4. $0.95 \times 10^{10}$ T4 virus particles + 0.201 mg *dl*-Bz-3-methyltryptophane. 5. $0.90 \times 10^{10}$ T6 virus particles. 6. $0.90 \times 10^{10}$ T6 virus particles + 0.204 mg *dl*-tryptophane. 7. $0.90 \times 10^{10}$ T6 virus particles + 0.201 mg *dl*-Bz-3-methyltryptophane. The turbidities of tubes were read at intervals on a Klett-Summerson Colorimeter (blue filter No. 42) and in the figure are plotted as ordinates against minutes after mixing plotted as abscissae.

seen that the methyltryptophane at 170 micromoles/liter is only slightly less active than *dl*-tryptophane itself at 185 micromoles/liter. These experiments show that Bz-3-methyltryptophane can take the place of tryptophane in the adsorption reaction between the viruses T4 and T6 and their host.

*Discussion.* Gordon and Jackson[8] showed that Bz-3-methyltryptophane can not replace tryptophane in the diet of the rat. Indeed, the death of three out of four animals fed diets in which Bz-3-methyltryptophane replaced tryptopnane suggested to them that the compound might be somewhat toxic. However, in further work they found that the substance had no effect on the growth rate of rats fed an adequate diet. The above experiments on the reversal of the methyltryptophane inhibition of *E. coli* growth by traces of tryptophane suggest that the tryptophane in Gordon and Jackson's complete diet for rats may have masked the detrimental effects of Bz-3-methyltryptophane.

The fact that Bz-3-methyltryptophane has almost the activity of tryptophane as a co-factor for T4 and T6 adsorption on their hosts is interesting from a number of standpoints. It indicates that this inhibitor of bacterial growth actually does perform the function of the structurally similar essential metabolite, tryptophane, in the reaction between the viruses T4 and T6 and their host. As to the function of the co-factor, it is not yet clear whether, as a cement substance, it acts in the specific combination between virus and host receptive spots or whether it acts as a sort of coenzyme in whose presence the virus particles, during their chance encounters with the host cells, are able to become attached to them and begin their parasitic activity. The high efficiency of Bz-3-methyltryptophane as a co-factor for the virus would suggest that the chain of essential reactions following virus adsorption does not involve the step which Bz-3-methyltryptophane blocks in the bacterial metabolism of tryptophane.

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## THE LOCAL ANESTHETIC PROPERTIES OF ISONIPECAINE

WHILE investigating the actions of isonipecaine, 1-methyl-4-phenylpiperidine-4-carboxylic acid ethyl ester hydrochloride, it was noted that the compound produced pronounced corneal anesthesia when it was applied to the rabbit eye. Although isonipecaine has been reported[1, 2] to abolish the wink reflex, the effect was produced after systemic administration. The

[8] W. G. Gordon and R. W. Jackson, *Jour. Biol. Chem.*, 110: 151, 1935.

[1] O. Schauman, *Arch. f. Exper. Path. u. Pharmakol.*, 196: 109, 1940.

[2] R. C. Batterman, *Arch. Int. Med.*, 71: 345, 1943.

action we obtained was essentially, a local one, and was not due to the central actions of isonipecaine.

Subsequent studies on the local anesthetic properties of isonipecaine revealed that it possesses considerable specificity for nervous tissue when applied locally. The drug was compared experimentally with an equal concentration of cocaine. The results of our preliminary studies are summarized in Table 1.

TABLE 1

LOCAL ANESTHETIC PROPERTIES OF ISONIPECAINE COMPARED WITH COCAINE

| Method (3) | Criterion | Drug | Minutes |
|---|---|---|---|
| Rabbit cornea | Duration of anesthesia | 1 % cocaine | 31 |
| | | 1 % isonipecaine | 19 |
| Intradermal wheal in man | Duration of anesthesia | 1 % cocaine | 78 |
| | | 1 % isonipecaine | 57 |
| Frog sciatic | Onset of sensory block | 1 % cocaine | 2.5 |
| | | 1 % isonipecaine | 2.6 |
| | Onset of motor block | 1 % cocaine | 13 |
| | | 1 % isonipecaine | 17 |

The fact that isonipecaine exhibits local anesthetic properties suggests that the compound may possibly be used advantageously as a preanesthetic agent for chloroform or cyclopropane anesthesia, and for operations involving the heart. There have been several recent reports[4, 5, 6] stating that the administration of certain local anesthetics depresses cardiac irritability. Consequently this depression results in a lessened tendency for cardiac disturbances during chloroform[7] or cyclopropane[8] anesthesia, and during operations on or near the heart.[4 5] Isonipecaine may possibly act in the same manner. In fact, the information at hand on the cardiac effects of isonipecaine favors this conclusion. Like others[1, 9] we have found that isonipecaine has a depressant action on the heart.

Also in the event of isonipecaine poisoning, it would seem logical to prevent or treat the overdosage with agents similar to those used in cases of local anesthetic toxicity. This suggestion is based on the fact that the chief toxic symptoms manifested in experimental animals after isonipecaine or local anesthetics administration are quite similar. These symptoms are referable to the central nervous system, consisting of restlessness and tremors which may proceed to clonic convulsions. For the treatment and prevention of poisoning by local anesthetics, Tatum and others[10, 11, 12] have indicated that the barbiturates are the preferable agents to employ.

These studies will be described in greater detail elsewhere. We have also initiated studies on the possible applications of isonipecaine suggested above, and we hope to report on them soon.

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# SCIENTIFIC APPARATUS AND LABORATORY METHODS

## INTRAVENOUS TUBING FOR PARENTERAL THERAPY

CONTINUOUS or frequently repeated intravenous treatment is often complicated by trauma and thrombosis to the extent that all available superficial veins become destroyed. The discomfort of numerous venepunctures may also become a serious problem, particularly in uncooperative or disoriented patients. These difficulties can largely be avoided by the use of flexible plastic tubing which can be inserted into a vein through a needle and left in place as long as required. This method has been used extensively on dogs in which the leg veins, external jugulars and even portal vein have been employed for continuous and intermittent infusions. In 11 dogs the tubes have remained in the external jugular veins for 4 to 5 weeks without untoward developments.

In 4 such dogs which were recently sacrificed for post-mortem study, the veins were thrombosed around the tube in 2, while in the remaining 2 the vein remained patent. Whether thrombosis is related to the mere presence of the catheter or to the irritating solution which was introduced daily through it has not yet been determined.

The following technique is recommended for patients. The skin over the vein to be used is anesthetized with procaine; a tourniquet is applied, and a 15-gauge needle is introduced. The flexible tubing is then threaded through the needle into the vein for a distance of 5 to 6 cm. The needle is removed over the tube, while the latter is held by pressure with the fingers over the vein. The point of entrance is covered with collodion and the free portion of the tubing

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