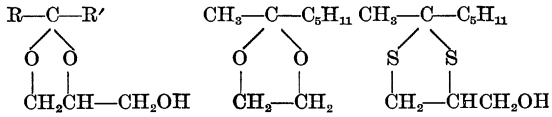
note is to show that these characteristic effects of the glycerol ethers on the central nervous system are also present in another series of compounds of quite different structure, the 2-substituted-4-hydroxymethyl-1,3-dioxolanes (e.g. I).



I, $R = CH_3$, $R' = n—C_5H_{11}$ II III

Preliminary examination of over 50 compounds (most of them new[2]) in this series showed that the type of physiological action obtained was markedly influenced by the groups in position 2. Some of the 2-alkyl and 2,2-dialkyl derivatives possessed a type of action similar to that of the monoethers of glycerol. Large doses of the active compounds caused complete muscular paralysis with a decrease of muscle tone. Spontaneous respiration and certain reflexes such as the knee jerk and wink reflex were maintained, even during profound paralysis. Small doses, which did not cause any detectable changes in the behavior and appearance of the animals, protected them from the effect of lethal doses of strychnine and Metrazol.

This paralyzing action appeared to be optimal if a total of 6–8 carbons was attached at position 2; the lower, water-soluble members of the series, and the higher, virtually water-insoluble members, were almost completely inactive. The compounds where R was methyl and R′ a straight-chain alkyl group of 5–7 carbon atoms were found definitely superior to those with a different combination of groups, even when the total number of carbons on the 2-position was constant. It is interesting to note that the substitution of a cyclohexyl group for the *n*-amyl or *n*-hexyl (I, $R = CH_3$, R′ = cyclohexyl) group decreased the activity sharply. Compounds in which R and R′ were part of a carbocyclic ring, *i.e.* derivatives of cyclopentanone and cyclohexanone, showed some paralyzing activity, but less than those in which R and R′ were alkyl groups.

The presence of the free hydroxyl group seemed to be essential for activity. The removal of the hydroxyl, as in II, or the acetylation of the hydroxyl of I abolished, or very markedly decreased, the paralyzing activity. The dithiolane III, analogous to I, was also inactive, as were the two examples of 2-substituted-4-hydroxymethyl-1,3-dioxolanes examined which contained a basic nitrogen atom. Compounds of formula I where R was alkyl and R′ was aryl or heterocyclic also possessed interesting pharmacological properties. Some of these compounds caused paralysis, whereas other closely related compounds caused tremors, hyperexcitability, and convulsions.

The dependence of the activity and toxicity on the size and nature of the alkyl groups in position 2 is illustrated in Table 1, which gives the mean paralytic and mean lethal doses of a few of the alkyl substituted compounds examined. (The dose which caused a loss of the righting reflex in 50% of the animals was taken as a measure of the relative activity of the compounds and was called the mean paralytic dose.) The table also gives the comparable values for myanesin (*o*-toloxy-1,2-propanediol), the best compound of the glycerol ether series. It will be noted that certain members of the dioxolane series possessed greater activity and a greater margin of safety than myanesin.

[2] We are indebted to J. Figueras, C. G. Krespan, L. Libermann, and F. C. Pennington for their work on the synthesis of these compounds. We are also indebted to R. Plato Schwartz, M.D., for his interest in this work.

TABLE 1

MEAN PARALYZING AND MEAN LETHAL DOSES OF CERTAIN 2-SUBSTITUTED-4-HYDROXYMETHYL-1,3-DIOXOLANES AFTER INTRAPERITONEAL ADMINISTRATION TO WHITE MICE

Formula I R	Formula I R′	$PD_{50} \pm SE$* (mg/kg)	$LD_{50} \pm SE$* (mg/kg)	LD_{50}/PD_{50}
n-C_3H_7	n-C_3H_7	205 ± 24	730 ± 69	3.6
i-C_3H_7	i-C_3H_7	155 ± 33	730 ± 73	4.7
n-C_6H_{13}	H†	153 ± 23	430 ± 53	2.9
CH_3	n-C_5H_{11}	105 ± 24	500 ± 31	4.8
CH_3	s-C_5H_{11}	190 ± 30	475 ± 56	2.5
Myanesin		180 ± 20	500 ± 43	2.8

* PD_{50} = mean paralyzing dose; LD_{50} = mean lethal dose; SE = standard error.

† This compound may have the 1,3-dioxan structure, which is a 6-ring isomeric with structure I. This structure has been excluded for the other compounds.

Certain compounds mentioned in this preliminary communication may be useful as tools in neurophysiological research; others have potential therapeutic application.

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A New Treatment of Viscosimetric Data[1]

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An interesting relationship exists in flow data secured from capillary-tube viscometers. To illustrate, Fig. 1 contains the flow data for several liquids obtained with a capillary-tube viscometer in which driving pressures were accurately controlled and expressed in millimeters of water. No kinetic energy corrections were applied. All of the flow lines look like those to be expected from such a study: they are logarithmic in type.

When two fixed pressures are chosen, as was done for Fig. 2—namely, at 100 and 500 mm of water pressure—and the two points for each liquid joined to form "two-

[1] This work was supported by the Johnson Research Fund of Northwestern University Medical School and the Evanston Hospital.

point flow lines," an unexpected harmony becomes evident; extrapolation of these lines results in the establishment of a *focal point*. When other pairs of pressures are taken in the same way, other focal points are

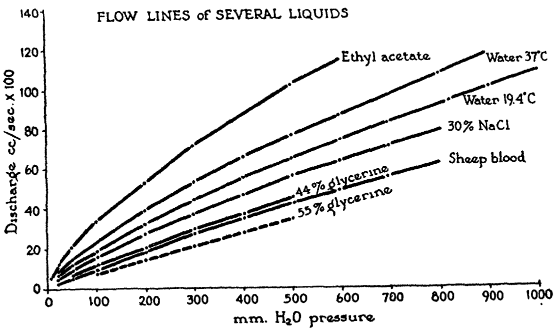

FIG. 1

established. All of these focal points appear to lie on a line passing through the origin.

Several valuable features arise from this observation. First, a given apparatus may be characterized by the slope of the line described by the focal points. Next, it is easy to determine whether a given liquid is flowing in a normal fashion. An example of an abnormally flowing liquid is blood: its two-point flow line does not reach the focal point established by normal liquids (Fig. 2).

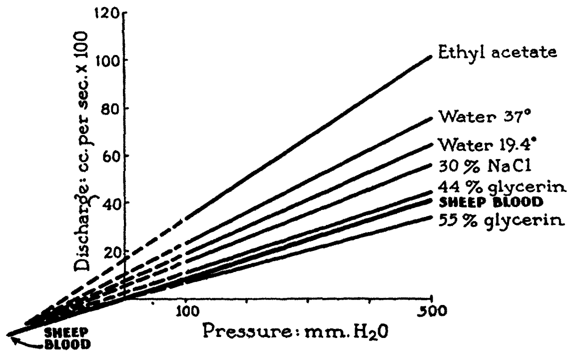

FIG. 2

Another advantage is that a single flow measurement will serve to define the whole logarithmic flow line of a normal liquid, since one point is already available in the focus and the curved line can be derived from the straight line thus determined.

The relationship described depends on the properties of the simple logarithmic curves traced by the flow lines. They belong to the type, $A \log X + B = \log Y$. These curves occur in families, each family with its own line of focal points passing through the origin if the treatment described above is applied. What seems remarkable is that normal liquids of a wide range of viscosity appear to flow through a given capillary in precisely the manner required to produce a group of flow lines that belong to a single family of logarithmic curves. A consideration of the known flow properties of normal liquids suggests that this is an effect to be anticipated.

Effect of Chemical Treatment Prior to Storage on Viability and Growth of Cottonseed

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Cottonseed having a moisture content of 8–11% can be stored without loss of viability (*8*) for periods as long as two years in most sections of the United States. Seed with a moisture content of 12% or above, however, present storage difficulties which depend on the climatic conditions existing in the locality in which they are stored. Investigations at the Southern Regional Research Laboratory on the applicability of chemical treatment in preventing or minimizing heating and deterioration of moist seeds stored in bulk prior to processing for oil and meal have demonstrated that a number of chemicals of various types are effective (*1–5*) for these purposes. Among these chemicals are propylene glycol dipropionate (PGDP) and 4,6-*bis*-chloromethyl xylene (DCB) (*6*).

It was of interest to determine whether these compounds could also be used to prevent loss of viability during storage of moist seed, and accordingly they were investigated separately and in mixtures. The preliminary results of storage experiments using a mixture of these two compounds are reported in this publication. A more detailed report will be presented at a later date.

A Stoneville 2B variety of cottonseed, harvested in 1946 and having an initial moisture content of 8.9% and a germination count of 92%, was artificially conditioned to a moisture content of 12%, as described in a recent publication (*7*). The conditioned seed was divided into three equal lots. The first lot was untreated and served as the control; the second was treated with 0.28% (based on the dry weight of the seed) of a solution of DCB in PGDP, in the ratio of 1:8 by weight; the third was treated with 0.14% of the same solution. All three lots of seed were stored individually in screw-top glass jars of 1-gal capacity which were maintained at room temperature in the dark. Samples of 50 seeds were withdrawn from each jar for the determination of germination counts and seedling growth at 30-day intervals over a period of 6½ months. Germinations were carried out by the standard blotter technique at room temperature, and the counts were recorded for 4-day-old seedlings. Growth measurements of various parts of all seedlings that germinated were made at intervals up to 12 days. During this period the seedlings were sup-

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[3] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, USDA.