standard inhibitor were tested further at several other concentrations. Since there was no a priori reason to expect that the inhibitors would be equally effective on heating and lipolysis, the relative efficiency of each inhibitor was determined with respect to both effects. The comparative effectiveness of a series of chemicals is shown in Table 2.

The data reveal the fact that a wide variety of chemicals in fairly low concentrations are capable of inhibiting heating and lipolysis in moist flaxseed.[4] Although flaxseed was used in all of the experiments, a number of the inhibitors listed in Table 2 have also been used in treating moist cottonseed, rice, and grain sorghum and have been found to be equally effective. The low concentrations at which many of these compounds were effective as inhibitors of heating and lipolysis suggest their use in treating seeds on an industrial scale to improve their storage properties. Mill-scale experiments to determine the effectiveness of a number of these inhibitors are in progress.

No attempt is made here to interpret the results presented above in terms of the relation between chemical structure and biological activity of the compounds examined to date. It is probable that although their net effect, namely, inhibition of heating and lipolysis, is the same, the mechanism whereby this inhibition is achieved in the seed may differ for each inhibitor. It is necessary, therefore, to investigate their effect on the components of the enzyme systems involved in heating and lipolysis before any conclusions can be drawn regarding the relationship between chemical structure and biological activity.

Other investigators (e.g. *6*) have attributed the heating and deterioration of grain to the action of microorganisms associated with the grain. As has been pointed out in a previous publication (*4*), heating and deterioration can be equally well ascribed to the enzyme activity within the seeds themselves. It is also possible that the enzymes both in the seeds and in the microorganisms are responsible, perhaps in different degrees, for the observed biological activity of the seeds. It has not been possible to conclude definitely what relative role is played by the enzymes from the two sources.

The objective of this research has been to develop improved methods of storage of seeds intended for industrial or food utilization in which preservation of viability is not important. It is recognized that the development of improved conditions for the storage of planting stock constitutes an equally important problem, and it is hoped that some of the results of these investigations may eventually be applied in storing seeds without loss of viability.

References

1. Altschul, A. M. *Oil Mill Gaz.*, 1944, **49**, 8, 13.
2. Altschul, A. M., Curet, M. E., Karon, M. L., Hall, C. M., and Smith, B. A. *Oil Mill Gaz.*, 1946, **50**, 9–13, 23.
3. Altschul, A. M., Karon, M. L., Kyame, L., and Caravella, M. *Oil & Soap*, 1943, **20**, 258–262.
4. Altschul, A. M., Karon, M. L., Kyame, L., and Hall, C. M. *Plant Physiol.*, 1946, **21**, 573–587.
5. Karon, M. L., and Altschul, A. M. *Plant Physiol.*, 1944, **19**, 310–325.
6. Milner, M., and Geddes, W. F. *Cereal Chem.*, 1946, **23**, 449–470.
7. Spiegelman, S., and Reiner, J. M. *J. gen. Physiol.*, 1945, **28**, 385–403.

---

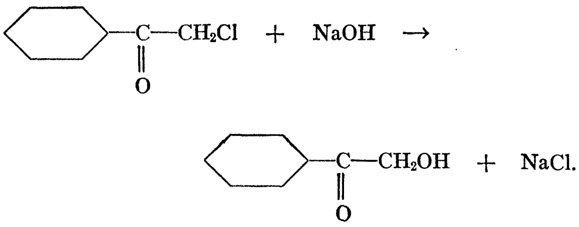
[4] In addition to the chemicals listed in Table 2, calcium propionate, glycol diacetate, diethyl malonate, and vinyl propionate have recently been found to act as inhibitors when used in concentrations equivalent to that of the ethylene chlorhydrin standard.

Hydrolysis by Carbitolic Caustic

R. Macy

Chemical Corps Technical Command,
Edgewood Arsenal, Maryland

Chloracetophenone (CN) has long been a popular lacrimator both for military and civilian uses. For example, it is a standard component of grenades employed by civilian police as well as by military forces. CN is characterized by rather high chemical stability, so that decontamination of an area covered by it can be accomplished by relatively few chemical treatments. One of the favorite points of attack on the molecule is the chlorine atom through hydrolysis by alkali:



Since CN is practically insoluble in water, the hydrolysis must be accomplished by employing the caustic in a solvent which will also dissolve the CN. Such a solvent is ethanol. A solution consisting of 5 per cent of sodium hydroxide and 95 per cent of ethanol will destroy a thin film of CN on a contaminated surface in a few minutes.

Because of the fire hazard introduced by ethanol in this decontaminating agent in certain military operations, a search was made for other mutual solvents for CN and sodium hydroxide. An added requirement for the solvent was that it should have good stability toward the alkali when the solution was stored. A large number of solvents were tested, and the search finally led to the following series of compounds:

(I)	$HOCH_2CH_2OH$	Ethylene glycol
(II)	$HOCH_2CH_2OCH_2CH_3$	Cellosolve
(III)	$HOCH_2CH_2OCH_2CH_2OH$	Diethylene glycol
(IV)	$HOCH_2CH_2OCH_2CH_2OCH_2CH_3$	Carbitol
(V)	$HOCH_2CH_2OCH_2CH_2OCH_2CH_2OH$	Triethylene glycol

As a result of these tests it was found that compound IV stood out quite sharply, not only for its solvent capacity for organic compounds but also for its stability toward alkali. The solubility of CN in dry carbitol at 22° C. was found to be 28.3 grams in 100 grams of solution, and in a mixture of 21 per cent of water and 79 per cent of carbitol (by weight) it was 9.3 grams in 100 grams of solution.

A solution containing, by weight, 5 per cent sodium hydroxide, 20 per cent water, and 75 per cent carbitol hydrolyzes CN quite rapidly when in thin film on an area. (In granular form CN dissolves rather slowly in carbitol, although it dissolves to a large extent, as already stated.) Higher concentrations of caustic can be used to give more rapid hydrolysis, but concentrations over 5 per cent may cause skin injuries unless personnel are well protected. The 5 per cent caustic solution in aqueous carbitol was found to be stable for at least two years in a sealed steel drum stored in the open without cover. It turns red on standing and absorbs the oxygen from the air in the container.

The principal object of this report is to bring carbitolic caustic to the attention of laboratory workers as a possible replacement for the well-known alcoholic caustic. There are probably many circumstances under which it should be a more desirable reagent. It is relatively nonflammable and can be used at temperatures considerably higher than the boiling point of ethanol if required to decompose a compound under reflux conditions.

Changes in Urinary Steroid Excretion and Correlated Metabolic Effects During Prolonged Administration of Adrenocorticotropic Hormone in Man[1]

George W. Thorn, F. T. Garnet Prunty,[2]
and Peter H. Forsham

Department of Medicine, Harvard Medical School, and
Medical Clinic, Peter Bent Brigham Hospital, Boston

Adrenocorticotropic hormone was administered to a 46-year-old male, known to have an expanding lesion involving the sella turcica which had been arrested by roentgen therapy. This subject was chosen because of the presence of signs and symptoms of moderate secondary adrenal-cortical insufficiency, which could be expected to accentuate any adrenotropic response to the pituitary hormone.

The adrenocorticotropic hormone was prepared from hog pituitary glands.[3] Two gamma of this preparation was found to give an adrenotropic response in the assay method of Sayers and Sayers (*1*). Electrophoretic analysis revealed the presence of more than one component. The material contains the equivalent of 0.12 unit of oxytocic activity/mg.; growth-promoting, gonadotropic, and thyrotropic factors are not present in significant amounts.

The patient was maintained on a constant diet and, after reaching a steady state, was given intramuscular injections of 10 mg. of A.C.T.H. every 6 hours for 6 days (40 mg. daily).

Some of the metabolic effects observed are shown in Fig. 1, in which the following changes should be noted: A 7-fold increase in the daily excretion of "11-oxysteroids," as estimated by a modification of the method of Talbot, *et al.* (*2*); an accompanying 5-fold increase in the 17-ketosteroid excretion; an increase of 58 per cent in the daily urinary output of total nitrogen, with a concurrent rise in the excretion of uric acid. Urinary creatinine remained constant from day to day. The excretion of sodium was markedly decreased throughout the period of administration.

The marked increase in the excretion of "11-oxysteroids" may be taken as definite evidence of increased adrenal-cortical activity under the action of the A.C.T.H. used. The rise in 17-ketosteroid output to as high a figure as 12.2 mg./day would indicate that the major part of this material was, in fact, derived from the adrenal cortex, since the maximum output by even normal testes is only of the order of 5 mg./day. The simultaneous changes observed in the excretion of both types of urinary steroid may be taken in support of either of two hypotheses: (1) that 17-ketosteroids derived from the adrenal cortex are formed to a considerable extent by the oxidative removal of the side chains of C_{21} steroids, the production of the latter being controlled by A.C.T.H.; or (2) that the anterior pituitary gland, through its A.C.T.H., stimulates the independent production of both C_{21} steroids and 17-ketosteroids, or related androgens, by the adrenal cortex.

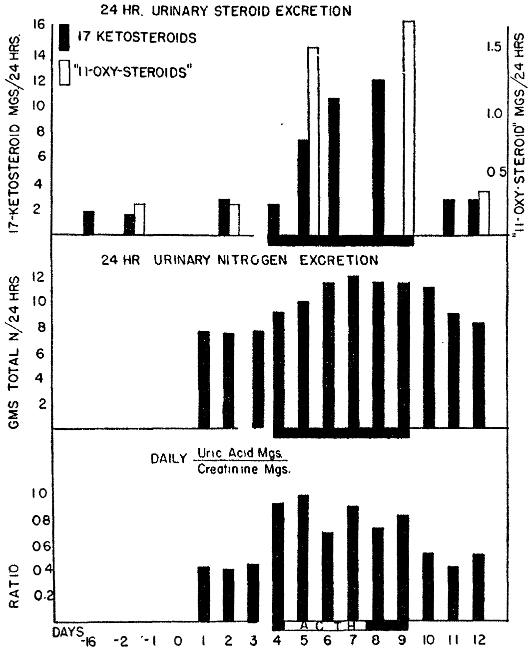


Fig. 1

The increased nitrogen excretion parallels that of the "11-oxysteroids," which are known to promote the catabolism of body protein, whereas the sodium retention suggests the elaboration of a desoxycorticosterone-like substance. From the close correlation between the observed changes in the urinary excretion of steroids, nitrogen, and uric acid, it appears useful to regard the ratio of uric acid to creatinine as a measure of increased activity of the adrenal cortex during a period of stimulation. This has been confirmed by experiments, being reported elsewhere, which include the demonstration that patients with primary adrenal-cortical insufficiency fail to show this response.

References

1. Sayers, M. A., and Sayers, G. *Fed. Proc.*, 1946, **5**, 200.
2. Talbot, N. B., Saltzman, A. H., Wixom, R. L., and Wolfe, J. K., *J. biol. Chem.*, 1945, **160**, 535.

---

[1] This study was aided in part by a grant from the Committee on Research in Endocrinology, National Research Council.

[2] Rockefeller Traveling Fellow.

[3] We are indebted to J. R. Mote, of the Armour Company, for a supply of the adrenocorticotropic hormone prepared in the Armour Laboratories.