The results indicate clearly that the glycuronic acid output may be decreased either by insulin or by phlorhizin. The normal output per rabbit after the above dose of menthol was about 4 grams of the crude ammonium menthol glycuronate. Under the same conditions, but with insulin and glucose, the output was only about 2.6 grams per rabbit. When starved and phlorhizinized, similar results were obtained, as in the case of insulin. This appears to indicate a relation between the amount of carbohydrate in the tissue and the extent of synthesis of glycuronate.

2979

Ketolytic action of various sugars in vitro.

T. E. FRIEDEMANN. (Introduced by P. A. Shaffer).

[From the Department of Biological Chemistry, Washington University School of Medicine, St. Louis, Mo.]

The results here summarized represent a continuation of the study of the *in vitro* reactions between sugars and acetoacetic acid discovered in 1921 by Shaffer[1] and are believed to afford an explanation of antiketogenesis.[2]

The reactions of aldehydes and sugars were studied under two conditions: (1) "non-oxidative" and (2) "oxidative".

"NON-OXIDATIVE REACTION."

Simple aldehydes such as formaldehyde,[3] acetaldehyde, glyoxylic acid, glyoxal,[4] and glyoxal carbonic acid reacted readily with potassium acetoacetate at pH 8.0 (in the absence of any oxidizing agent). *Under the same conditions only simple aldoses reacted.* Thus glycol aldehyde and glyceric aldehyde reacted with acetoacetate. *Dihydroxy acetone* did not react and in this respect it acted like other ketones such as pyruvic acid and acetone. How-

---

[1] Shaffer, P. A., *J. Biol. Chem.*, 1921, xlvii, 433.

[2] Shaffer, P. A., *J. Biol. Chem.*, 1921, xlvii, 449.

[3] Shaffer, P. A., "Antiketogenesis: Its Mechanism and Significance." *Harvey Society Lectures*, 1923-1924. Lippincott Company, Philadelphia.

[4] Shaffer, P. A., and Friedemann, T. E., *J. Biol. Chem.*, 1924, lxi, 585.

ever, when the solution of dihydroxy acetone was made strongly alkaline it reacted as readily as glyceric aldehyde, showing that rearrangement of the inert ketone form are necessary before reaction may occur. The more complex sugars, the pentoses and hexoses, did not react in non-oxidative neutral media, but they became reactive in strongly alkaline solutions,[5] the alkali perhaps opening the ring and producing the free aldehyde form of sugar which latter form is active in a manner similar to glycol- and glycer-aldehydes.

Although these reactions occurred in dilute solution (20 millimols aldehyde : 80 millimols acetoacetate per liter) they were more rapid and extensive in concentrated solution. In concentrated solutions the total acetoacetate consumption approached two molecules for each molecule of added aldehyde, never greater than two. In the case of acetaldehyde, where it was possible to determine both aldehyde and acetoacetate consumption, a similar 1 to 2 ratio was found. This again shows the similarity to the Knovenagel reaction.[4]

TABLE I.

33.4 mMols. Acetaldehyde + 102.3 mMols. K acetoacetate per liter. 23 hrs. in water bath at 37.5° C.

	millimols
Acetaldehyde consumed	15.4
Acetoacetate consumed	28.3
CO_2 liberated as $KHCO_3$	32.1

"OXIDATIVE REACTION."

Twenty millimols of aldehyde or sugar were oxidized by 200 millimols H_2O_2 in 0.5 N KOH in the presence of 80 millimols potassium acetoacetate. *It was found that only those sugars which reduced Fehling's solution were ketolytically active.* Aldehydes, even though some of them (glyoxylic acid and glyoxal carbonic acid) reduced Fehling's solution, were inactive. Dihydroxy acetone, which in non-oxidative solutions was inert, became exceedingly reactive, its reaction rate coinciding with glyceric aldehyde.

The reaction rates for glycol- and glyceric aldehydes, which were very much greater in the oxidative medium, and dihydroxy acetone, did not show an initial lag such as was always found in the case of the pentoses, hexoses, heptoses, and polyoses. This lag, in the case of the sugars possessing ring structures, showed

---

[5] Friedemann, E. E., *J. Biol Chem., Proc.,* 1925, lxiii, 21.

TABLE II.

In 1000 cc. 37.5° C. { 20 mMols. Sugar; 500 cc. "purest" KOH
75-80 mMols. K Acetoacetate; 200 mMols. H_2O_2

		Acetoacetate consumed by one mol. of sugar*
Diose:	Glycol aldehyde	1.9
Triose:	Glycer aldehyde	2.2
	Dihydroxy Acetone	2.2
Pentose:	l-Arabinose	2.7
	l-Xylose	2.7
Hexose:	d-Glucose	2.4
	d-Fructose	2.3
	d-Mannose	2.1
Heptose:	d-Glucoheptose	2.2
	Mannoketoheptose	2.7
Disaccharoses:	Maltose	2.0
	Lactose	1.8
	Sucrose	.2

* These results represent the total consumed in 12 hours minus the blank. Thus 20mMols. dihydroxy acetone consumed 54.6 mMols. acetoacetate, of which 9.9 were calculated to be due to *direct* oxidation. The amount consumed by the sugar was therefore 54.6–9.9, or 44.7.

that an opening of the ring or other transformations are necessary before reaction may occur. This open-ring, reactive form is probably the substance which condenses with aceto acetate, it is believed. That the sugar molecule as a whole, and not a fragment, participates in the condensation, is the only conclusion one may draw from the data shown in Table II.

2980

On conduction of the action potential wave through the dorsal root ganglion.

JOSEPH ERLANGER, GEO. H. BISHOP and H. S. GASSER.

[*From the Department of Physiology and the Department of Pharmacology of Washington University, St. Louis, Mo.*]

It has been reported[1] that the action potential wave started by stimulation of the sciatic nerve arrives in the dorsal roots of that nerve somewhat later than in its ventral roots. Further experi-

---

[1] Erlanger, J., Bishop, G. H., and Gasser, H. S., *Am. J. Physiol.*, 1925, lxxii, 197.