TABLE I.
Summary of Data Showing Relationship of Plasma Concentration and Urinary Excretion to Adrenolytic Activity of C-7337.

Dose, mg/kg	No. of animals	% of dose recovered in urine		Blockade of epinephrine pressor effect		Mean peak plasma level, γ/ml	
		Free	Total	Onset min.	Duration in hr	Conc., γ/ml	Min. after administration
				Intravenously			
1.	7	8.5	12.4	<2	2	<1.0	—
4.	6	8.7	12.9	<2	10	8.7	0–5
15.	8	13.8	23.3	<2	18	8.3	0–5
				Orally			
6.25	6	2.6	5.4	120	2	<1.0	—
25.	7	4.9	13.9	15	12	1.2	15–30
100.	7	4.3	10.4	15	18	4.0	15–30

been obtained as to the metabolic fate of C-7337 or the nature of the conjugated material which can be detected in the urine. A small amount of impure hydrolyzed metabolic product has been collected and tested for its pharmacological action. The concentration of the material used for these biological tests was determined in terms of material which coupled with 4-amino-antipyrine. It was found that this metabolic product did possess adrenolytic action, although it was less than ¼th as active as an equal amount of pure C-7337 and was shorter in duration of effect. Since the material isolated was not pure the only conclusion which can be drawn from these experiments is that some of the metabolic products have lost their effectiveness as adrenolytic agents.

Summary. 1) A chemical method is described for the determination of C-7337 in plasma and urine which is sensitive to at least a concentration of 2 γ/ml.

2) In terms of duration of blockade of epinephrine pressor effect, C-7337 is approximately 1/5th as active by mouth as by intravenous injection.

3) Approximately 10% free C-7337 may be recovered in the urine following intravenous injection whereas only one half this amount may be recovered after oral administration.

4) C-7337 disappears rapidly from plasma but continues to be present in the urine for as long as 24 hours. These results indicate that the drug is extensively localized in some tissues of the body.

Received January 20, 1950. P.S.E.B.M., 1950, v73.

Interference by Glucose in the Quantitative Determination of Uric Acid.* (17685)

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A notable increase in uric acid and glucose excretion was observed in a patient with juvenile rheumatoid arthritis (Still's disease) while receiving cortisone and also when given ACTH. The parallelism between observed values of uric acid and glucose was impressive and suggested the need to check the effect of glucose on the values obtained for uric acid by the method used. The method for the determination of uric acid was that of Buchanan, Block and Christman(1) in which uric

* This work is part of a study supported by a grant from the Masonic Foundation for Medical Research and Human Welfare.

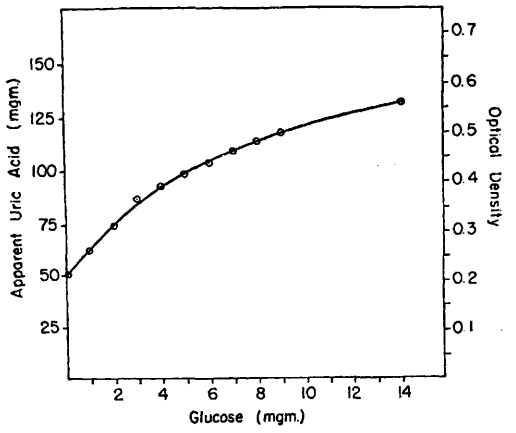

FIG. 1.

Effect of increasing glucose concentration on a constant amount of uric acid. 50 μg of uric acid in 50 ml of water. Read at 660 μ in a Coleman junior spectrophotometer.

acid is determined as the difference in values obtained before and after digestion with the enzyme uricase. Application of this method to solutions of uric acid, of glucose, and of mixtures of uric acid and glucose gave the following results:

a. Color formation from given amounts of glucose and of uric acid in mixtures of the two was far greater than that found when either was used alone.

m. After the step of digestion with uricase, neither glucose nor uric acid reduced the reagent to form color.

Fig. 1 illustrates the effect of adding increasing amounts of glucose to a constant amount of uric acid. In urine which contains a normal amount of uric acid and a 4% glucose concentration, on proper dilution, the urine aliquot would give a reading about 80% higher than could be accounted for by the amount of uric acid alone, as that aliquot would contain 4 mg of glucose.

Further study of the uricase procedure disclosed that the loss of reducing action of glucose was due to the borate buffer. When a carbonate buffer was substituted for the borate in the uricase digestion, it was found that the reducing action due to glucose was not destroyed, indicating the hydrogen ion concentration was not a factor. If borate buffer is added to mixtures of uric acid and glucose before color development, the reducing action of glucose is suppressed. This is illustrated by the data in Tables I and II which show the results obtained on the addition of borate to pure uric acid solutions as well as to urine. Loss of reducing action of glucose to alkaline copper solutions in the presence of borate was reported by Levy(2,3). Levy demonstrated that this was due to the formation of a borate glucose complex.

In conclusion, glucose in the presence of uric acid reduces arsenophosphotungstic acid to a much greater extent than it does alone. The usual conditions of uricase incubation are such that a glucose borate complex is formed with a loss of the reducing action of the glucose. Since in the method of Buchanan, Block and Christman borate is only added to the aliquot treated with uricase, but not to the one used for the total color determination, er-

TABLE I.

Effect of Glucose and Borate on the Uric Acid Determination.

(Uric acid 50 μg; glucose 4 mg; borate buffer at pH 9.2 (Clark Pg. 201) 3 ml in 50 ml of water). Read in a Coleman Junior Spectrophotometer at 660 μ.

Contents of tube	Glucose	Uric acid	Glucose + Borate	Uric Acid + Borate	Uric Acid + Glucose	Uric Acid + Glucose + Borate
Total Chromogen as μg Uric Acid	9.5	50.	0.	48.7	95.2	50.
After incubation of each of the above with uricase and subtraction of the uricase blank.						
Residual Chromogen as μg Uric Acid	2.	0.5	2.	0.5	1.5	1.5
Apparent "True Uric Acid"	7.5	49.5	—	48.2	93.7	48.5

1. Buchanan, Block, and Christman, *J. Biol. Chem.*, 1945, v157, 181.
2. Levy and Doisy, *J. Biol. Chem.*, 1928, v77, 733.
3. Levy and Doisy, *J. Biol. Chem.*, 1929, v84, 749.

TABLE II.
Changes in Total and Residual Chromogen in Urine.
(10 ml of normal urine diluted 1:10; 4 mg glucose added, and 3 ml borate buffer in 50 ml of water).

Contents of tube	Urine	Urine + Borate	Urine + Glucose	Urine + Glucose + Borate
Total Chromogen as μg Uric Acid	53.9	53.6	97.4	54.4
After the incubation with uricase, and borate buffer.				
Residual Chromogen as μg Uric Acid			8.6	8.6
Apparent "True Uric Acid"			88.8	45.8

roneously high values result. Addition of borate to both the aliquot treated with uricase, and to the total color determination eliminates the interference of glucose.

Received January 23, 1950. P.S.E.B.M., 1950, v73.

Effect of Vitamin B_{12} on Experimental Hepatic Injury.* (17686)

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Observations on the effect of crude liver extract in experimental hepatic injury in rats have been previously reported(1-3). It has been shown that liver extract given by mouth is without influence on, or will even promote the development of acute diffuse hepatic necrosis. On the other hand, liver extract will not only prevent cirrhosis but has a definitely beneficial effect in the treatment of hepatic cirrhosis. Thus, the effect of liver extract may be comparable to that of choline, the latter also having a beneficial effect on cirrhosis, and no effect or a deleterious one on necrosis(1,4,5). The fact that the combination of liver extract with methionine or with protein proved to be superior in the treatment of experimental cirrhosis(3) to the effect of methionine or protein alone seemed to indicate that the beneficial effect of the liver extract might not have been due to its content of choline but perhaps to some other constituent, such as vitamin B_{12}. This supposition was based on the assumption that choline, methionine and protein (caesin) all act similarly as sources of "labile methyl" and it was difficult to believe that a simple increase in supply of the same factor over and above a sufficient supply could have improved the therapeutic results as distinctly as was seen on the addition of liver extract to methionine and protein.

In the course of their studies on the lipotropic effect of liver extract Hall and Drill(6) reached similar conclusions. They found liver extract a much more potent lipotropic agent

* This represents work carried out under the auspices of the Commission on Liver Disease of the Armed Forces Epidemiological Board, Office of the Surgeon General, U. S. Army, Washington, D.C.

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