Timed Excretion of 5-Hydroxy Indoleacetic Acid after Oral Administration of Bananas and 5-Hydroxytryptamine. (24406)

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Recent investigators(1,2) have reported the presence of relatively high concentrations of 5-hydroxytryptamine (5-HT), or serotonin, in pulp and peel of bananas. The increased excretion in urine of the major metabolite of 5-HT, 5-Hydroxyindoleacetic acid (5-HIAA), following ingestion of bananas has some clinical significance. Proper evaluation of abnormally high values for 5-HIAA in human urine, as determined either by a quick screening procedure(3) or a quantitative method (4), requires consideration of the subjects' dietary intake during a period preceding the collection of urine samples. Failure to consider this factor will lead to confusion in the (laboratory) diagnosis of malignant carcinoid tumors(5). Duration of the influence of ingested 5-HT on 5-HIAA excretion has not been defined. The factors determining degree and duration of the effect of banana (or 5-HT) ingestion include rate of absorption from the gastrointestinal tract, rate of deamination of 5-HT by monoamine oxidase, and subsequent excretion of 5-HIAA. There is reason to believe that both rate of conversion of 5-HT and renal clearance of 5-HIAA are quite rapid(6). With regard to absorption of 5-HT from the gastrointestinal tract, Page(7) states that "nothing is known." For this reason, an attempt was made to define the period during which the level of 5-HIAA in urine may be elevated following a single dietary exposure to 5-HT.

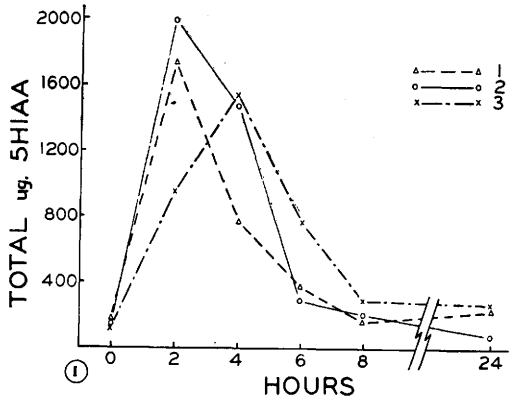
Methods. 1. Three adult healthy male subjects were fed between 300-500 g of banana pulp in less than 30 minutes, approximately 3 hours after the breakfast meal. A 16-hour urine sample was obtained just prior to ingestion of the bananas. Following this, urine samples were collected every 2 hours for a total of 8 hours. A second 16-hour urine sample was then obtained. The volume of each urine sample was recorded and an aliquot used for determination(4) of the quantity of 5-HIAA present. Urines were kept frozen during the delay between collection and analysis, which was in the order of 24-72 hours for each experiment. 2. Time-excretion curves of 5-HIAA in the same 3 subjects were determined following ingestion of a known quantity of 5-HT. To facilitate comparison, an oral dosage of 10,000 μg of 5-HT (21.9 mg of 5-HT-creatinine sulfate)* was administered. This was dissolved in 100 ml of distilled water and consumed over a 10-minute period. Solutions were made up just prior to use. Urine collections and analyses were carried out exactly as before except that the fourth collection period was 3 instead of 2 hours. 3. Daily fluctuation in 5-HIAA excretion was studied in these 3 subjects. Other than elimination of bananas from the diet one day before and during the period of urine collection, no dietary restrictions were imposed. An initial overnight control sample and urine from 4 collection periods of 3 hours each were handled as previously described.

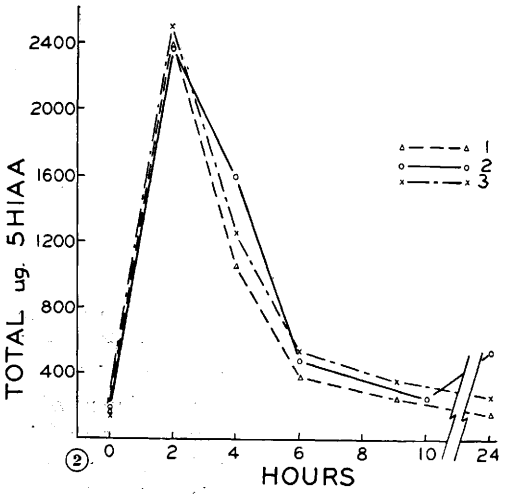
Results. Fig. 1 shows time-excretion relationships of 5-HIAA following banana pulp for all 3 individuals. (Subjects 1 and 2 consumed bananas from the same stalk. The fruit fed to Subject 3 was obtained at a later date.) A rough estimate of total 5-HT ingested was calculated using the average value of 28 μg of 5-HT/g of pulp as reported by Waalkes *et al.*(2).

An approximation of the increase in total 5-HIAA excreted in the first 8 hours after ingestion of bananas was obtained by subtracting the average quantity of 5-HIAA/hour in the control period from the hourly excretion rates after bananas.

Table I presents data for subjects, as to quantity of pulp consumed, estimated total 5-HT intake, total 5-HIAA excretion (above "normal"), and also expressed as estimated percent of 5-HT ingested appearing in urine as its metabolite during an initial 8-hour period.

* Provided by Abbott Laboratories.





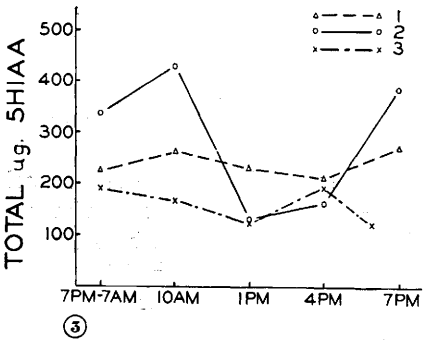


FIG. 1. Excretion patterns of 5 HIAA after bananas.

FIG. 2. Excretion patterns of 5 HIAA after oral administration of 10 mg 5-HT.

FIG. 3. Daily fluctuation in excretion of 5 HIAA.

Fig. 2 illustrates time-excretion curves of 5-HIAA seen after oral administration of 10,000 μg of 5-HT. Subject 2 inadvertently forgot the elimination of bananas from the diet and consumed a banana cream custard at 7 p.m. on day of experiment. This is responsible for the secondary rise in 5-HIAA excretion seen in the last sample. Table II summarizes data on total excretion of 5-HIAA and percentage of 5-HT metabolized and eliminated in 8 hours (actual collection was 9 hours).

TABLE I. Metabolism of 5-HT Consumed in Banana Pulp.

	Subject		
	1	2	3
G pulp consumed	414	380	361
Total 5-HT intake, mg (estimate)	11,592	10,640	10,108
Total 5-HIAA excretion (incr.), mg, 8 hr	6,130	7,950	7,020
% metabolized and excreted in 8 hr	48.7	68.0	64.4

Fig. 3 shows daily variation in excretion of 5-HIAA under "normal" conditions.

Discussion. Considering first the result of 5-HT oral administration, on the basis of this limited study, 5-HT is absorbed very rapidly from the upper gastrointestinal tract. In the fasting state, absorption is essentially complete. This is based upon previous studies(6, 8) indicating that conversion of 5-HT to 5-HIAA accounts for the major pathway of the metabolism of 5-HT. In all 3 subjects total increase in 5-HIAA excreted in 8 hours equals about 60-70% of the ingested 5-HT. Excretion curves also support the very high renal clearance of 5-HIAA seen in animals(6).

Similarity in excretory patterns after banana and 5-HT ingestion suggests that the serotonin present in banana pulp is rapidly available for absorption. The effect of consuming bananas on 5-HIAA levels in urine should be minimal about 8 hours after ingestion.

TABLE II. Metabolism of Orally Administered 5-HT.

	Subject		
	1	2	3
Total 5-HT intake, mg	10,000	10,000	10,000
Total 5-HIAA excretion (incr.), mg, 8 hr	6,656	7,980	7,800
% metabolized and excreted in 8 hr	61.2	73.4	72.5

The only symptom recorded by the participants was mild abdominal cramping shortly after consuming the 5-HT solution in Subject 1.

While the basic "normal" level of 5-HIAA varied in the subjects, all exhibited its increase in the post-prandial urine specimens, especially those collected after morning and evening meals. The source of this increase is not known.

Summary. Absorption of 5-HT, including that present in banana pulp, is quite rapid and fairly complete. Conversion to 5-HIAA and renal excretion of this metabolite are accomplished without delay. In evaluating abnormally high levels of 5-HIAA in human urine the dietary history is of some significance. Urines obtained more than 8 hours after ingestion of bananas should show little influence of exogenous 5-HT administration.

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Metabolic Acidosis in the Alligator.* (24407)

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In the course of experiments to determine the effect of epinephrine on carbohydrate metabolism in the alligator(1), it was noted that the quantity of lactic acid produced by glycolysis often exceeded the extracellular bicarbonate reserves available to neutralize it. Although one might expect the alligator to experience acidotic coma, blood pH was often only slightly below normal. It was evident that some accessory mechanism for neutralizing organic acids must have been available to prevent a fatal acidemia. Development of a severe lactic acidosis does not occur in the mammal because lactate is metabolized almost as fast as it is produced. In contrast the alligator is placed in a precarious state by a combination of a rapid rate of muscle glycogen breakdown combined with a slow rate of lactate utilization(1). This phenomenon provided a unique opportunity to study the compensatory mechanisms employed by an animal made acutely acidotic by its own tissues and not by injected salts or inorganic acids.

Methods. For this study 50 alligators weighing from ½ to 3 kg were injected intramuscularly with USP epinephrine in doses of 1 mg/kg. Blood and urine specimens were collected at intervals and were analyzed by methods previously described(1,2). Since theophylline exerts many similar effects to those resulting from epinephrine(3), several alligators were also injected with this compound.

Results. Paradoxically, the better the nutritional state of an alligator, the greater the danger from epinephrine or theophylline induced acidosis. In alligators with ample muscle glycogen stores the lactate rise was great, but in those in poor condition the response was less. In those animals whose plasma lactate increased by 20 mEq/l or more or whose blood pH fell below 6.8, one in 10 died.

Fig. 1 shows average plasma changes following injection of 1 mg of epinephrine/kg into 5 well nourished alligators. Numerically the lactate rise exceeded the bicarbonate fall

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