Serotonin content of foods: effect on urinary excretion of 5-hydroxyindoleacetic acid[1-3]

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ABSTRACT Using a highly specific radioenzymatic assay we determined the serotonin concentration in 80 types of foods. The following fruits had a high serotonin concentration (mean ± SEM) expressed in μg/g weight: plantain 30.3 ± 7.5; pineapple 17.0 ± 5.1; banana 15.0 ± 2.4; Kiwi fruit 5.8 ± 0.9; plums 4.7 ± 0.8; and tomatoes 3.2 ± 0.6. Only nuts in the walnut or hickory family had a high serotonin concentration expressed in μg/g weight: butternuts 398 ± 90; black walnuts 304 ± 46; English walnuts 87 ± 20; shagbark hickory nuts 143 ± 23; mockernut hickory nuts 67 ± 13; pecans 29 ± 4; and sweet pignuts 25 ± 8. Ingestion of these fruits and nuts resulted in an increase in urinary 5-hydroxyindoleacetic acid excretion with no change in platelet serotonin concentration. The above foods should not be eaten while a urine is being collected for 5-hydroxyindoleacetic acid analysis. *Am J Clin Nutr* 1985;42:639-643.

KEY WORDS Serotonin, 5-hydroxyindoleacetic acid, carcinoid syndrome, nuts, fruits, urine tests

Introduction

Many carcinoid tumors and occasional oat cell carcinomas (small-cell carcinomas) produce serotonin. As patients harboring such tumors have an increase in the urinary excretion of 5-hydroxyindoleaceticacid (5-HIAA, the principal metabolite of serotonin), the quantitative urinary excretion of this metabolite is the most useful way to diagnose serotonin overproduction (1).

It is reported that some foods contain substantial quantities of serotonin and that ingestion of these foods might increase the urinary excretion of 5-HIAA beyond the normal range in the absence of a serotonin-producing tumor. Foods reported to contain a high concentration include banana (2), tomatoes (3), plantain (4), red plums (4), avocado (4), eggplant (4), pineapple (5), and English walnuts (6). Most protocols for the collection of 24-h urine for 5-HIAA analysis advise patients not to eat these foods during the time that they are collecting the urine.

The studies evaluating the serotonin content of foods were performed over 24 yr ago when the state-of-the-art analytical methods included spectrophotometry, fluorometry, and paper chromatography. In the most extensive of these studies, the serotonin concentration of only 12 fruits and vegetables was determined (4). In the present study we determined the serotonin concentration of over 80 foods using a highly specific analytical technique that combined radioenzymatic analysis and thin layer chromatography. We also determined the effect of eating some of the serotonin-rich foods on urinary 5-HIAA excretion and platelet serotonin concentration.

Subjects and methods

Eight healthy subjects (5 women, 3 men) ranged in age from 21 to 49 yr (mean age 32 yr). None of the subjects were ingesting any medications. During control studies they ate their conventional diet; they then supplemented their conventional diets with serotonin-rich foods. The 24-h urine specimens, which were collected without preservative, were maintained at 3°C throughout the collection period. The procedures followed were in accord with the

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ethical standards of the Committee on Human Experimentation of Duke University.

The foods were purchased from commercial outlets; some of the nuts were obtained directly from local trees. The foods were homogenized in phosphate buffer (0.01 M; pH, 7) and processed as one would process a tissue (7, 8). They were analyzed by a radioenzymatic method in which serotonin is converted to N-acetylserotonin with acetic anhydride; the N-acetylserotonin is converted to tritiated melatonin using [^{3}H]S-adenosyl-L-methionine (New England Nuclear, Boston, MA) and hydroxyindole-O-methyltransferase that was partially purified from bovine pineal glands (7, 8). Following isolation by thin layer chromatography, the tritiated melatonin is quantitated by liquid scintillation spectrometry. The coefficients of variation are: intrassay 7% and interassay 13%. The cross-reactivity of the following compounds with serotonin is all less than 0.15%: tyramine, tryptamine, histamine, β-phenylethylamine, dopamine, n-acetyldopamine, epinephrine, norepinephrine, and 5-hydroxytryptophan. The lower limit of assay sensitivity (counts/min twice blank) is 10 pg of serotonin. The values for foods with low or moderate serotonin concentration represent the mean of two samples of food; the values for foods with a high serotonin concentration and avocados represent the mean ± SEM of four to six samples of food.

Platelet serotonin was measured by radioenzymatic analysis and was expressed per mg platelet protein (9). Urinary 5-HIAA excretion was measured with a spectrophotometric method (10). Statistical analysis was performed by standard techniques (11).

TABLE 1
Serotonin concentration of fruits and vegetables

High Serotonin (>3.0 μg/g)	
Plantain	30 ± 7.5 μg/g
Pineapple	17.0 ± 5.1
Banana	15.0 ± 2.4
Kiwi fruit	5.8 ± 0.9
Plums	4.7 ± 0.8
Tomatoes	3.2 ± 0.6
Moderate Serotonin (0.1 to 3 μg/g)	
Avocados	
Haas (California)	1.6 ± 0.40
Fuerte (California)	1.5 ± 0.21
Booth (Florida)	0.2 ± 0.04
Dates	1.3
Grapefruit	0.9
Canteloupe	0.9
Honeydew melon	0.6
Olives (Black)	0.2
Broccoli	0.2
Eggplant	0.2
Figs	0.2
Spinach	0.1
Cauliflower	0.1

Results

Plantain, pineapple, banana, Kiwi fruit, plums, and tomatoes had a high (>3.0 μg/g) serotonin concentration (**Table 1**). The serotonin concentration of red (5.7 μg/g), blue-red (3.6 μg/g) and blue (4.3 μg/g) plums were comparable and were grouped together.

Ten fruits and vegetables had a moderate (0.1 to 3.0 μg/g) serotonin (Table 1). The serotonin concentration of Haas and Fuerte avocados was seven times greater than that of Booth avocados (Table 1).

The following fruits and vegetables had a low (<0.1 μg/g) serotonin concentration: strawberries, blueberries, raspberries, cranberries, pomegranate, persimmon, apple, crabapple, cherries, papaya, mango, grapes (Tokay), pear, peach, orange, tangerine, lemon, lime, kumquat, radish, carrots, green beans, bell pepper (red), cucumber, lettuce (Iceberg), asparagus, lima beans, corn, peas, soybeans, and peanuts.

We analyzed the fruits and vegetables when they were of proper ripeness for eating. However, the serotonin concentration of bananas and plantain did not seem to be different in ripe and unripe fruit.

Table 2 shows that all of the nuts in the walnut and hickory families had an extremely high serotonin concentration. There was no difference in the serotonin concentrations of English walnuts and pecans in the shell as compared to the serotonin concentration of these nuts packaged after removal from the shell indicating that the serotonin concentration was probably relatively stable even after shelling.

Seven types of nuts had a moderate (0.1 to 3.0 μg/g) serotonin concentration. Of these, filbert and Brazil nuts contained 2.1 and 1.3 μg/g serotonin respectively. The serotonin concentration of almonds, beech nuts, cashew nuts, coconuts, and Macadamia nuts ranged from 0.2 to 0.6 μg/g.

The following nuts and seeds had a low (<0.1 μg/g) serotonin concentration: American chestnuts, pistachio nuts, pine nuts, horse chestnuts, buckeye nuts (yellow), acorns (white and red oaks), nutmeg, and sunflower seeds.

The following miscellaneous foods had a low (<0.1 μg/g) serotonin concentration: beefsteak (broiled), ham (baked), chicken (baked), fish (broiled), Parmesan cheese, corn,

TABLE 2
Nuts with high (>3.0 μg/g) serotonin

Walnut Family	
Butternuts (Juglans cinerea)	398 ± 90
Black walnuts (Juglans nigra)	304 ± 46
English walnuts (Juglans regia)	87 ± 20
Hickory Family	
Shagbark (Caraya ovata)	143 ± 23
Mockernut (Caraya tomentosa)	67 ± 13
Pecans (Caraya illinoensis)	29 ± 4
Sweet Pignuts (Caraya ovalis)	25 ± 8

potatoes, rice, and wheat germ. The following beverages had a low (<1 μg/ml) serotonin concentration: coffee, tea, milk, beer, and Chianti wine.

Table 3 depicts the distribution of serotonin in various areas of fruit. The serotonin concentration of fruit peel is high in banana and plantain, but low in pineapple, Kiwi fruit, and tomatoes. The serotonin concentration is higher in the center area that contains seeds in banana and plantain but not in the seed-containing areas of Kiwi fruit, tomatoes, and avocado. The serotonin concentration is higher in the soft edible edge of pineapple than in the less palatable center core.

Figure 1 shows that when seven normal subjects eat a conventional diet their 5-HIAA excretion is 4.8 ± 0.6 mg/24 h. When they supplement their diet with four medium-size bananas, their 5-HIAA excretion increases to 15.3 ± 0.6 ($p < 0.01$). After eating four bananas, all of the normal subjects have 5-HIAA excretion that is in the range found in patients with serotonin-producing carcinoid tumors; however, their platelet serotonin concentration (pmol serotonin/mg platelet protein) ranged from 631 to 1,835 (mean ± SEM, 1134 ± 200) with all subjects within the normal range of 300 to 2,200 pmol/mg.

Table 4 demonstrates that dietary supplementation with black walnuts, pineapple, or plantain also increases the urinary excretion of 5-HIAA into the abnormal range. When the meat from 32 black walnuts was ingested, the 5-HIAA excretion was more than seven times greater than the upper limits of normal. The serotonin concentration of plantain probably remains high even after this vegetable is fried, for a volunteer eating two fried plantains had a threefold increase in 5-HIAA excretion. The platelet serotonin concentrations of all the subjects who ingested the foods tabulated in Table 4 remained with normal limits.

Discussion

Using a highly specific radioenzymatic method of serotonin analysis, we have confirmed that banana, plantain, pineapple, red plums, blue-red plums, and English walnuts, as reported, have a high concentration of serotonin (1–6). We have found, however, that the serotonin concentrations of tomatoes and eggplant, is only 27% and 10% respectively of the previously reported concentrations (4).

TABLE 3
Distribution of serotonin in areas of fruit

Fruit	Serotonin
	μg/g
Banana	
Peel	31.8
Pulp—Slice	14.0
Pulp—Center	26.6
Pulp—Edge	6.3
Plantain	
Peel	17.4
Pulp—Slice	20.0
Pulp—Center	27.7
Pulp—Edge	8.8
Pineapple	
Pulp—Edge	31.5
Core—Center	8.7
Peel	2.7
Kiwi Fruit	
Pulp—Edge	6.8
Pulp—Center	3.0
Peel	0.3
Tomatoes	
Pulp	3.7
Seeds	3.2
Peel	0.8
Avocado—Haas	
Pulp	1.10
Seed	0.06

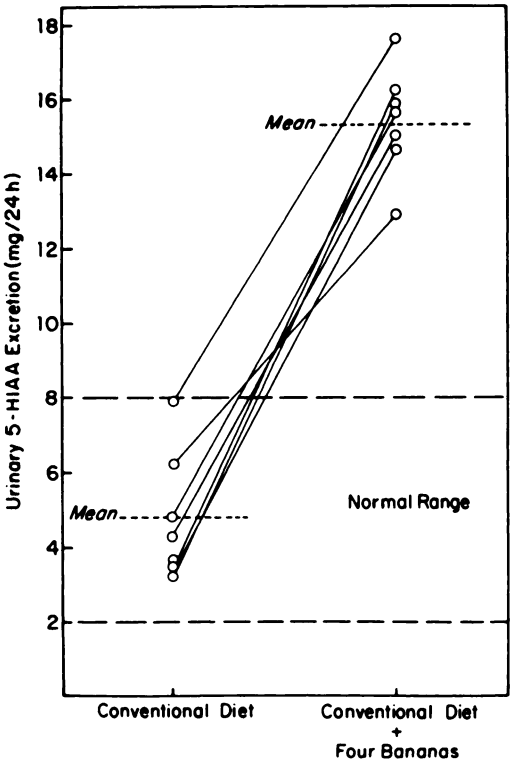

FIG 1. Urinary 5-HIAA excretion of seven normal subjects. Addition of four medium-size bananas caused a significant elevation in urinary 5-HIAA excretion ($p < 0.01$). The 5-HIAA of individual subjects are connected by a line.

Our studies also result in some new additions to the list of serotonin-rich foods. These include Kiwi fruit (Actinidiae sinesis, Chinese gooseberry), which has become a popular fruit in the United States in the last 5 yr, and blue plums. We also noted that the extremely high serotonin concentration in nuts is not limited to English walnuts but is found in all members of the walnut and hickory families we tested. With the exception of filbert and Brazil nuts that had a serotonin concentration of 2.1 and 1.3 μg/g respectively, all other nuts had a serotonin concentration of less than 1.0 μg/g.

Although the varietal was not noted, avocado was reported to contain a serotonin concentration of 10 μg/g (4). We found that the least expensive and most frequently sold Booth varietal contained only 2% (0.2 μg/g) as much serotonin as previously reported. The more flavorful and usually more expensive varietals, such as the Fuerte and Haas avocados contained only 16% as much serotonin as reported. We did not notice this difference in the serotonin concentration of varietals of other fruits such as oranges (Navel, Temple) or tomatoes (cherry, standard-size).

Our data demonstrating that foods with high serotonin concentrations are limited to certain fruits and nuts contrasts with our observations on the distribution of histamine in food (12). A high concentration of histamine is found in a fruit (eggplant), a vegetable (spinach), and in some foods produced by microbial action (Parmesan, Roquefort, and blue cheese; Chianti wine). We do not know if serotonin has a physiological role in the fruits and nuts in which it is concentrated. It is of interest that indoleacetic acid, a closely related compound,

TABLE 4
Alteration in urinary 5-hydroxyindoleacetic acid excretion following ingestion of serotonin-rich food

Subject	Food	Quantity ingested	Urinary 5-HIAA excretion†	
			Conventional diet	Supplement with serotonin-rich food
		g	*mg/24 h*	
1	Black Walnuts (32)*	100	7.0	59.0
2	Black Walnuts (16)*	50	3.7	26.0
1	Pineapple (1/2)*	510	6.0	12.0
3	Pineapple (1/4)*	358	2.1	8.1
1	Fried Plantain (2)*	400	5.5	18.4
1	*Mixed Diet*		5.3	37.2
	Black Walnuts (10)*	30		
	Banana (1)*	100		
	Kiwi fruit (1)*	30		

* Number of units of food ingested.
† Normal range 2–8 mg/24 h.

is a potent physiological growth regulator (auxin) in many plants (13).

Although the urinary 5-HIAA excretion was markedly increased by ingesting serotonin-rich food for 1 day, there was no increase in the platelet serotonin concentration. This is probably due to the conversion of serotonin to 5-HIAA by the high levels of monoamine oxidase present in gastrointestinal mucosa and liver (14). When normal volunteers ingested massive doses of serotonin (160 mg/d) for 5 days in the form of the pure chemical, there was an increase in both urinary 5-HIAA and platelet serotonin (14). Although it no longer appears to be a major health problem, at one time endocardial fibroelastosis was prevalent in Uganda (15). Speculation was that the ingestion of large quantities of serotonin in bananas and plantain might have played a role in this endocardial fibroelastosis. There is, however, no evidence that moderate amounts of serotonin-rich foods have any adverse effect on the health of well-nourished people. The senior author, who incidentally is subject one in Table 4, continues to eat and enjoy bananas, plantain, pineapple, Kiwi fruit, tomatoes, plums and walnuts.

Based on the weight of the edible fruit pulp or nutmeats in a medium-size specimen and the mean serotonin concentration of the fruit or nut, one would have to eat the following portions of food to raise the urinary 5-HIAA excretion 1 mg/24 h: one butternut or black walnut, one and a half English walnuts, eight pecans, one-sixth of a plantain, one-half of a banana, one-twentieth of a pineapple, one and one-fifth tomatoes, two Kiwi fruits, two red plums or five and one-half Haas or Fuerte avocados. We therefore recommend that patients collecting a 24-h urine for 5-HIAA analysis avoid these foods. In contrast one would have to eat 10 eggplants or 170 filbert nuts to increase the urinary 5-HIAA excretion 1 mg/24 h. Clinically, there is an inverse relationship between the length of a list of things patients should avoid and their success in avoiding them. Thus we do not advise patients to avoid such foods as eggplants and filbert nuts while collecting the 24-h urine specimen for 5-HIAA analysis.

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